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SLEEPING SICKNESS.

MACLEAN (G.). **A Report on Human Trypanosomiasis in Tanganyika Territory for the Year ending 31st December, 1927.**—*Tanganyika Territory Ann. Med. & San. Rep. for Year ending 31st December, 1927.* pp. 129–138.

The infected regions of the Territory are still divided into the five following separate areas :—

(1) The Maswa-Ikoma area ; Mwanza Province.
(2) The Tanganyika Lake Shore area ; Kigoma Province.
(3) The Ufipa-Tabora area ; partly in Kigoma and partly in Tabora Province.
(4) The Liwale area ; Lindi Province.
(5) The Rovuma area ; partly in Lindi and partly in Mahenge Province.

During the year the only serious spread occurred in the Ufipa-Tabora area, where the disease appears to be making progress northwards. In a table the number of new cases discovered during 1927 and the number of deaths recorded are given in respect of each of the five areas. In all, 360 new cases were found and 148 deaths occurred during the year. In addition, it is noted that 22 deaths took place during 1926, but were not recorded until 1927. With the possible exception of Southern Ufipa, all the available evidence points to a man-fly-man spread ; and even in Ufipa it is not necessary to assume the existence of a vertebrate host other than man. On the other hand, the author adds that it is not suggested that non-human vertebrate hosts have been excluded, or that they may not be an active epidemiological factor. Examples are given in support of these contentions.

The next section of the report describes in detail the general sleeping sickness policy ; and the text of the Memorandum, dated August 22nd, 1927, the general principles of which have been approved, is given in full.

Turning to treatment, the author states that the results obtained with the 1924 and 1925 cases formed the subject of a later report.

In Rhodesian cases it was found that Bayer 205 alone does fairly well in early cases, and in cases whose general symptoms are chronic or slight. Probably the best prognostic criterion is the condition of the cerebro-spinal fluid after a course of treatment. A cell count of 30 or less per cmm. appears to be a good prognostic sign and an indication that treatment may cease. Fourneau 309 was used in a very limited number of cases, with apparently the same results as with Bayer 205. Try-

parsamide alone has given good results in a few cases, but the general verdict is that it is unsatisfactory. Combined Bayer and tryparsamide treatment is now on trial and the results obtained suggest that, provided treatment is commenced with Bayer 205, the combination is more effective in the average case than with either drug singly.

In *gambiense* cases it is impossible to record this year any observations of value.

An account is next given of the situation in the sleeping sickness areas. In Maswa-Ikoma area the extent of country known to be infected was considerably increased during the year. This may be a genuine spread, but is more likely to be the gradual unveiling of the situation. In the Tanganyika Lake Shore area, the situation has remained unchanged. In the Ufipa-Tabora area a new outbreak—probably a spread from known foci, though this has not been established—was discovered about forty miles north west of Tabora towards the end of the year. The outbreak is serious in that it strikes at an important labour supply area. The only measure carried out so far is the treatment of patients. A resettlement scheme will be put forward as soon as the necessary agricultural information is available. In the Liwale area the most interesting point was a recrudescence of the incidence of the disease in two circumscribed regions, which were well known to the Medical Officer, Dr. DYE. [See this *Bulletin*, Vol. 25, p. 331.]

The general preventive measures adopted are the segregation and treatment of all infected cases and the clearing of scrub around villages, particularly infected villages, so as to make them fly-free. No cases were reported from the Rovuma area during the year, but there is no reason to believe that the disease has died out, and had staff been available for the survey there is little doubt cases would have been found.

W. Yorke.

MACLEAN (George). **The Relationship between Economic Development and Rhodesian Sleeping Sickness in Tanganyika Territory.**—*Ann. Trop. Med. & Parasit.* 1929. Apr. 26. Vol. 23. No. 1. pp. 37–46. With 1 diagram & 1 map. [3 refs.]

The following summary is given :—

"Before the days of European domination the people of Tanganyika Territory lived for the most part under conditions which made it difficult for Rhodesian sleeping sickness to get a firm footing.

"The freedom that followed the coming of the European resulted in the evolution of a type of bush family village which became a danger to health because of the close contact between man and tsetse that it made possible.

"Some of the old large settlements shrank to the dimensions of these villages from various causes, the chief of which were the disturbances produced by the Great War and the re-distribution of population that has resulted from the opening up of the country.

"The situation can be met by encouraging native agriculture where this can profitably be done. In places so remote that successful development is problematical the people can be collected in settlements large enough to be safe from extinction by trypanosomiasis. The people in these settlements have a tendency to drift towards places where better conditions prevail. When this takes place on a large scale the dwindling settlements will have to amalgamate for self-protection, a process of gradual and orderly evacuation will have set in, and continue unless some local attractive source of wealth is discovered to turn the tide.

"Once the bush village is compulsorily eliminated it should be possible for reclamation and evacuation to go on in an orderly fashion, as the exigencies of the general situation demand. It should also be possible for native and non-native enterprise to go on with no more antagonism than a legitimate rivalry for labour and for markets."

W. Y.

CORSON (J. F.). **Sleeping Sickness in the Ikoma District of Tanganyika Territory; Notes on Some Cases treated by Professor F. K. Kleine.** —*Ann. Trop. Med. & Parasit.* 1928. Dec. 28. Vol. 22. No. 4. pp. 379–417. [15 refs.]

The cases referred to were, for the most part, suffering from Rhodesian sleeping sickness, and were treated by KLEINE between September, 1926, and May, 1927. Corson continued the work on more or less similar lines during the following five months, and from October, 1927, to June, 1928, he was succeeded by Park NOBLE. The principle of treatment was the combined use of germanin with preparations of arsenic and antimony. Before discussing the cases, the author refers briefly to certain associated conditions. Amongst the other diseases prevalent were malaria, relapsing fever and, probably, syphilis. Helminth infections were very rare. Game animals were abundant throughout the area all the year round. Two species of Glossina were present, viz., *G. swynnertoni* and *G. pallidipes*, the former being much the more numerous. Tsetses are, as a rule, rarely encountered in the valleys, and large numbers of cattle, sheep, and goats are kept. The people are well-nourished; they are much addicted to hunting, and make farms in the bush at considerable distances from their villages. Their customs bring many natives into close contact with tsetse under conditions favourable to the transmission of sleeping sickness.

The author considers that the natural duration of the disease in untreated cases is about six months to a year. He knows of no case of natural recovery. Diagnosis was chiefly made from stained thick blood films, and in nearly all cases trypanosomes were easily found at the first examination. The author states that he was not always able to be sure of the infection of the central nervous system from clinical signs unless these were very definite. Weakness and wasting may develop very quickly in Rhodesian sleeping sickness.

Most of the patients presented the clinical picture of an acute illness with considerable wasting and weakness, some fever, headache, general body pains, and enlargement of the lymphatic glands; localized swelling or oedema was present in a few cases. As many patients, on temporary recovery, were allowed to visit their homes re-infection could not be absolutely excluded. Tsetse were rarely seen in the precincts of the hospital. In a table it is shown that parasitic blood relapses nearly always occur within a few months of the cessation of treatment, and sometimes during treatment. They were almost always associated with symptoms.

Writing on the effects of the drugs used, the author states that the general experience is that there is no drug which can be compared in value with Bayer 205 in the treatment of early Rhodesian sleeping sickness; and he adds there seems to be no reason why a white person should, in future, die of the disease. Natives however, unfortunately, usually come for treatment in a later stage. The question whether Bayer 205 acts beneficially on the infected nervous system is very

important. Much has been written suggesting that it does not, and reference to the author's protocols shows that some of these cases have died and many have relapsed after a course of treatment that would be regarded as very thorough in early cases. On the other hand, the progress of certain cases suggests that the drug has an effect, direct or indirect, on the infection of the central nervous system. At any rate, it appears to reduce the virulence of the trypanosomes at least for a long time.

Tryparsamide has not given results in any way comparable with the success gained for it in *T. gambiense* infections. In previously untreated cases, it failed to cause trypanosomes to disappear from the peripheral circulation sometimes after the administration of a considerable number of doses. The general conclusion reached is that this drug should be used in succession to, and not instead of, Bayer 205.

"BR68." This is a preparation of arsenic made by BINZ and RÄTH. It is stated to be one of a number of preparations in which arsenic is combined with pyridin or chinolin groups. The drug was given intravenously in two relapsed cases. The clinical effects and action on the blood were good, but in one of the cases it did not appear to influence the infection of the central nervous system.

Various antimony preparations, such as stibosan and antimosan, were not found to be very satisfactory. Details of the cases treated are given in tables.

W. Y.

TROLLI (G.). La trypanosomiase au Congo Belge en 1927. [**Trypanosomiasis in Belgian Congo in 1927.**]—*Bull. Office Internat. d' Hyg. Publique.* 1929. Feb. Vol. 21. No. 2. pp. 285–303. With 1 map.

The author gives an account of the present position as regards sleeping sickness in the Belgian Congo. The results of examination of large numbers of the population in the various provinces are summarized in the following table :—

	Examined.	*Punctured.*	*New Cases.*	*Old Cases.*	*Total on treatment.*
Prov. Congo-Kasai ...	1,063,516	123,812	14,530	59,606	31,492
Province Equateur ...	180,523	21,751	1,583	4,066	3,306
Province Orientale ...	213,786	47,260	362	5,193	5,621
Province Katanga ...	166,014	2,500	1,335	800	2,349
Terr. Ruanda-Urundi...	80,638	3,347	1,266	1,278	2,544
Total	1,704,477	198,670	16,260	70,940	45,359

At Lusanga the itinerant medical service, composed of a doctor and a sanitary agent, have examined 82,572 persons and found 68 patients and two in the sleeping sickness stage. These figures must be added to those of the total above. The patients on treatment, roughly 45,500, referred to in the table are really those on treatment at the end of the year ; they comprise the new cases and the old cases subjected

to a second or to a third course of treatment. At the end of three months a certain number of cases enter their rest period and are replaced by others who have finished their period of rest. By this means, with cases diagnosed recently, approximately the same numbers of patients are on treatment all the year round. A summary is given of the situation in the various divisions of the Provinces. The summary is mainly statistical and should be consulted by those interested. Fourteen cases of the disease were diagnosed amongst Europeans—six at Katanga in the Tanganyika-Moero District, and eight in the Province of Congo-Kasai of which six were at Leopoldville West, one at Bas-Congo and one at Kwango. In addition, two cases were found among the missionaries at the Swedish mission on the north Cataracts. None of these patients have died. It is universally agreed that tryparsamide should replace old methods of treatment. There is no more efficacious method of treatment at the moment and this fact if fully recognized by the natives. Financial problems prevent its general use. The question of the re-opening of the old lazarets also arises; examination of the cerebro-spinal fluid and the admission to hospital of all cases exhibiting pathological changes in the fluid are necessary.

W. Y.

LASNET. L'organisation de la lutte contre la maladie du sommeil dans les colonies françaises de l'Afrique. [**Organization of Anti-Sleeping Sickness Measures in the French African Colonies.**]—*Bull. Office Internat. d'Hyg. Publique.* 1929. Feb. Vol. 21. No. 2. pp. 279–284.

In the French African Colonies sleeping sickness exists: (1) In Equatorial Africa in the greater part of its extent from the coast up to Fort Lamy along the banks of the Chari. (2) In the Cameroons: in the basins of the Haut-Nyong and the Doumé. (3) In Haut-Togo. In West Africa a number of other circumscribed foci have been known for many years, in particular in the Senegal and Casamanca and in Guinea. These do not appear to extend.

The author then passes to a consideration of the organization of sleeping sickness services. He states that in the Cameroons this consists of an autonomous mission comprising 10 doctors, 20 European sanitary agents and 300 native assistants. In Equatorial Africa the service has been reorganized in the form of a mission consisting of 11 doctors, 1 veterinarian, 10 hygienists, 12 European sanitary agents and 105 native assistants. In Togo the situation has not necessitated the creation of a special mission. A doctor with a number of native assistants deals with situations in the various parts of the colony. A statement of the expenditure devoted to trypanosomiasis in the various colonies during the past few years is set forth in a table. The prophylactic measures adopted are three-fold.

(*a*) Administrative measures relating to the carriers of the virus; this is called medical prophylaxis.

(*b*) Destruction of the haunts of Glossina; this is known as agronomic or administrative prophylaxis.

(*c*) The treatment of the sick. Details are given of each of these lines of action.

W. Y.

SUDAN: **Report on Sleeping Sickness by the Principal Medical Officer, Sudan Defence Force for the Periods 1st October, 1926 to 31st December, 1926 and from 1st January, 1927 to 31st December, 1927.** [MAURICE (G. K.) Acting P.M.O.]—*Rep. on Med. & Health Work in the Sudan for the Year 1927.* pp. 29–32.

In a table the admissions into hospital for sleeping-sickness from Mongalla and the Bahr El Ghazal during each of the years 1909–1927 are given. The figures show that sleeping sickness is no longer epidemic in the Sudan. Only 33 cases were found in Tembura as against 839 in 1923. A very brief account is given of the situation in each of the sleeping sickness districts. The author states that the situation can be summed up as follows:—

"1. Sleeping Sickness is under complete control in the Sudan.

"2. The people throughout the fly areas are closely administered and situated in villages inimical to sleeping sickness. Therefore, a serious epidemic is unlikely to occur again ever, provided inspections are regular.

"3. The disease could quite easily be stamped out definitely if there were not heavily infected countries along 1,000 miles of Sudan frontier.

"4. Things being as they are the complete eradication of sleeping sickness from the Sudan is impossible and a close watch has to be kept to detect local outbreaks.

"5. If local outbreaks are not detected an epidemic will result.

"6. Since a considerable staff has to be employed to detect local outbreaks some relaxation of existing regulations at the present time is permissible, but only because adjoining countries make permanent eradication impossible.

"7. The staff, employed primarily for sleeping sicknes, is by no means confined in its activities to sleeping sickness, but is able effectively to deal with many diseases, which in other circumstances would take a heavy toll of the population."

W. Y.

HOFFMANN (C. C.). [Kurze Beschreibung eines vermutlichen Ueberträgers der menschlichen Trypanosomiasis im Staat Veracruz.] [**Short Description of a Probable Vector of Human Trypanosomiasis in Vera Cruz.**]—*Rev. Mexic. de Biol.* 1928. Vol. 8. [Summarized in *Arch. f. Schiffs- u. Trop.-Hyg.* 1929. May. Vol. 33. No. 5. p. 304.]

The author believes that *Conorrhinus dimidiatus* Latr. is possibly an invertebrate host of *Trypanosoma cruzi.* The insect extends as far as 20° N. in Mexico, but only in the eastern portion of the country. Two sub-species are found, viz.: *C. dimidiatus dimidiatus* Latr. and *C. dimidiatus maculipennis* Stal. Hitherto only the latter has been recognized as an ectoparasite of man. The district of Vera Cruz is not very different from those in which Chagas disease is found. *Dasypus novemcinctus* Latr. and *Didelphys virginiana* Kerr. are also found at Vera Cruz. However no definite case of trypanosomiasis has been recorded in Mexico. Probably this is due to the fact that both insects live in the woods and are parasites of wild animals and are not yet adapted to man. In inhabited regions *C. dimidiatus* is rarely encountered. Developmental forms of the trypanosome are met with in the insects, but have never been found in man.

On the contrary, *C. dimidiatus maculipennis* was found by the author in clefts in the walls of old houses in Vera Cruz. In this situation they are apparently well adapted to man and bite frequently at night.

W. Y.

JOHNSON (W. B.) & LESTER (H. M. O.). **The Value of the Adhesion Phenomenon in estimating Wild Game "Trypanosome Reservoirs" and as an Aid to Diagnosis in Human Trypanosomiasis.**—*West African Med. Jl.* Lagos. 1929. Jan. Vol. 2. No. 3. pp. 144–156. With 1 chart. [6 refs.]

Acting on the suggestion of DAVIS and BROWN, 1927, the authors have examined the value of the adhesion phenomenon in estimating wild game-trypanosome reservoirs, and as an aid to diagnosis in human trypanosomiasis. An account of the technique is given. The trypanosomes used in the experiments were: *T. brucei* (strains B and C obtained from wild *Glossina morsitans*), *T. gambiense* (strain C obtained from a case of human trypanosomiasis), and *T. congolense* (strain D obtained from wild *Glossina morsitans* and strain E obtained from a naturally infected dog).

Preliminary experiments confirmed the specificity of the adhesion phenomenon in animals immunized against trypanosome infections. The reaction did not occur in animals naturally non-susceptible to a strain of trypanosomes when tested against this strain. For example, 32 human sera tested against *T. brucei* all gave negative results. Human and rat sera tested against *T. congolense* also gave negative results. Application of the test to animals showing chronic infection of trypanosomes gave positive results.

The reaction has been obtained in the blood of wild game when tested against *T. brucei* and *T. congolense.* The test is thus likely to be of value in estimating "trypanosome reservoirs" and may throw light upon the nature of the game immunity to trypanosomes. It may be of value in distinguishing between "game infective" and "human infective" strains of trypanosomes and in determining the part played by animal hosts as reservoirs of sleeping sickness. The authors consider the test should also be effective for demonstration of chronic trypanosome infection in cattle, sheep, and goats, etc., in which it is known that such infections may lie dormant for considerable periods until adverse conditions reduce the animal's resistance and cause the disease to assume a suddenly acute and fatal form.

Two hundred cases diagnosed as sleeping sickness were tested against *T. gambiense* by the adhesion test. As controls, three African cases of syphilis and seven normal European bloods were used. All the controls gave negative results. Sixteen cases of human trypanosomiasis which gave positive results against *T. gambiense* were also tested against *T. brucei* and gave no reaction. Details of all the cases tested are shown in a table. The cases were grouped as follows:—

Group I. Before treatment.
,, *II.* During treatment.
,, *III.* Within one year after treatment.
,, *IV.* From 1 to 3 years after treatment.
,, *V.* From 3 to 5 years after treatment.

Group I.—Of these, 31 cases gave positive results, 3 were doubtful and 6 were negative. Of the 6 negative cases, 5 have been diagnosed on clinical signs only, and the diagnosis was probably incorrect, but one had trypanosomes in the gland juice. Limiting the observations to the 30 cases of this group which had been proved microscopically to be sleeping sickness, it was found that 90 per cent. were positive, 6·7 per cent. were doubtful, and 3·3 per cent. were negative.

Group II.—Of the cases in this group 39 gave positive results, 2 doubtful, and 5 negative. Of the 37 cases proved positive microscopically, 86·5 per cent. gave positive reactions, 5·4 per cent. were doubtful, and 8·1 per cent. were negative.

Group III.—51 cases belonging to this group gave positive reactions, 2 were doubtful and 8 were negative. Of the 51 cases proved positive microscopically, 84·6 per cent. gave positive reactions, 3·8 per cent. were doubtful, and 11·6 per cent. were negative.

Group IV.—In this group, 27 cases gave positive results, 8 were doubtful and 13 were negative. Of the 45 cases proved microscopically to be infected before treatment, 57·8 per cent. gave positive reactions, 15·5 were doubtful, and 26·7 were negative.

Group V.—Only 5 cases in this group were available and all had been proved microscopically to be infected before treatment. One gave a doubtful reaction and the remainder were negative.

The authors consider that the test is of real value for diagnosis in human trypanosomiasis. The reaction gradually disappears after a varying period following infection and treatment. It is suggested that the test is an indication of acquired immunity and that, as this is lost, re-infection may occur. It is considered that the test is more reliable than the formol-gel test in cases of human trypanosomiasis.

W. Y.

MÜHLENS (P.). Trypanosomiasis bei Mutter und Säugling. [**Trypanosomiasis in Mother and Suckling.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1929. Mar. Vol. 33. No. 3. pp. 181–187. [7 refs.] [Inst. for Ship & Trop. Diseases, Hamburg.]

A detailed account is given of the medical history of a mother and infant, both of whom suffered from trypanosomiasis. The mother was presumably infected in Angola at the beginning of 1925. She left for Germany in May, 1925. No parasites were found, however, until October. The patient remained in good condition. From November 6th to 10th she was given a course of 4 gm. of germanin. A short time afterwards she had a nasal operation followed by erysipelas and then a relapse of trypanosomiasis. A second course of germanin was given. She returned to Africa in April, 1926, and on the voyage had fever and was given an injection of 1 gm. of germanin by the ship's doctor. Shortly after her arrival in Africa she had further fever with erythema and great loss of weight. No information is available regarding her further treatment, but it is known that, in the third stage of sleeping sickness, she had injections of germanin shortly before her death which occurred 12 days after the birth of a child on October 19th, 1927.

The medical record of the child shows that on November 6th, 1927, it was very anaemic, in poor condition and suffering from periodic attacks of fever. A blood film was examined, but no trypanosomes were seen. Notes made on various other occasions between this date and April 8th, 1928, when the infant left for Germany, record attacks of fever, erythemas, and oedemas. Enlargement of the cervical lymph glands was first noticed on February 21st, 1928.

On admission to hospital at Hamburg a few trypanosomes were found in the blood, the temperature was normal, the weight was 6·5 kgm. and the general intelligence and development satisfactory. There was no enlargement of the lymphatics and the internal organs were normal.

On May 5th, 1928, a course of treatment with germanin was commenced. The child apparently did well until the end of October, but in November it was taken ill and admitted to hospital at Leipzig with pronounced nervous symptoms. It was treated with tryparsamide and died suddenly on January 19th, 1929.

The author reviews the evidence relating to the question whether this was a case of congenital infection and concludes from the available facts that it probably was.

W. Y.

GRAF. Beitrag zur Pathologie des Glossina palpalis-Stichs und der Inkubationszeit bei Schlafkrankheit. [**Pathology of** *Glossina palpalis* **Bite. Incubation Period in Sleeping Sickness.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1929. Apr. Vol. 33. No. 4. pp. 219–222.

On November 18th, 1928, the author in the Cameroons was consulted by a patient who complained of a boil. On the left side of the face, directly under the ear, was a round inflamed area about 3 cm. in diameter: in the middle of it was a red spot almost 1 cm. in diameter, surrounded by a waxen zone about 3-4 cm. in breadth having the appearance of a confused mass of minute vesicles, and this again was surrounded by a red zone; the surrounding tissue was swollen. The lesion itself was hard and felt like a button embedded in the tissues, and was very painful. The temperature was 39° C. and the pulse 100. The patient stated that the trouble started two days previously as a small pimple: the following day he had a temperature and a slight rigor and the pain was greater. During the evening of November 17th, the symptoms became remarkably increased in severity.

The patient himself considered the lesion to be a boil, and did not remember being bitten by an insect, but another European recalled its striking similarity to the tsetse bite in a European (FELDMANN) in the same area two years previously, who subsequently developed trypanosomiasis.

The author punctured the inner margin of the white zone and in a stained preparation found numerous trypanosomes. The two following days trypanosomes were again found in the lesion. It is important also to note that on the last occasion, i.e., only four days after the commencement of the lesion, trypanosomes were found in the finger blood. The patient was treated immediately with "Bayer 205" with the result that the lesion at once subsided.

On November 23rd, the author was consulted by another patient who had heard of the previous case and who had 28 days previously been bitten by a tsetse on the right temple. The lesion was slightly red and painful, especially on pressure; it increased slowly in size reaching its maximum on the third day after which it slowly subsided. The whole process lasted 5 days, during which the patient had some fever and headache. Examination of the finger blood on the eighth day revealed the presence of trypanosomes.

W. Y.

HANSCHELL (H. M.); NEWHAM (H. B.): **The Initial Lesion of Sleeping Sickness.** [Correspondence.]—*Lancet.* 1929. June 1. p. 1170.

Both writers point out that, before 1910, MANSON taught that the indurated inflammatory lesion which developed at the exact site of, and

surrounding, the tsetse bite, and sometimes persisted for many weeks, signified an *infective* bite. Newham observed two similar cases during the War in East Africa. Hanschell points out that notwithstanding MANSON's teaching, reference to his initial lesion is absent from the text books.*

W. Y.

RAMON GINER (D.). Puede hacerse cronica la enfermedad del sueño? [**Is there a Chronic Sleeping Sickness?**]—*Medicina Países Cálidos.* Madrid. 1929. Jan. Vol. 2. No. 1. pp. 66–68.

The author gives brief details of three patients, and states that he has histories of eleven, met with in Fernando Po, in whose blood trypanosomes had been present—" *T. gambiense* or one of its allies "—for 18 months or more, without producing any signs clinically. They show no glandular enlargements and appear to be in good health, physically and mentally.

H. Harold Scott.

NIÑO (Flavio L.). A propósito de un nuevo caso de enfermedad de Chagas en la República Argentina. (Consideraciones sobre su diagnóstico etiológico). [**Another Case of Chagas's Disease in the Argentine and its Diagnosis.**]—*Prensa Méd. Argentina.* 1928. Dec. 20. Vol. 15. No. 20. pp. 869–872. With 3 text figs. [4 refs.]

This is interesting as an example of " latent " Chagas's disease. The patient was a married woman of 38 years presenting the ovarian type of the affection—metrorrhagia, flushings of the face, nausea, insomnia, throbbing in the head, swelling of the thryoid, excess of hair on the face. Examination of the blood revealed no trypanosomes, but quartan malaria parasites. Her blood was inoculated into laboratory animals, and though the blood of the latter was examined frequently during three and a half months no parasites were found in it. One was then killed and its tissues sectioned. Masses of the *Trypanosoma cruzi* were found in the kidneys and in the striated muscles; there were signs of myocarditis, but no parasites in the heart-muscle. The chief point is that examination of the blood alone, of the patient or of the inoculated animal, was insufficient to establish the diagnosis.

H. Harold Scott.

GEOGHEGAN (A.). A propos d'un nouveau cas de trypanosomiase humaine américaine dans la ville de Catamarca. [**Case of American Trypanosomiasis in the Town of Catamarca (Argentine).**]—*C.R. Soc. Biol.* 1929. Jan. 18. Vol. 100. No. 2. p. 137.

In October, 1928, the author saw a Catamarcan child seven months old with very violent convulsions which terminated by paroxysms of spasmodic rigidity. Large numbers of *Trypanosoma cruzi* were found in the peripheral blood. The Triatoma captured in the house were heavily infected, about 80 per cent. harbouring metacyclic trypanosomes.

W. Y.

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* This statement, as Dr. MANSON-BAHR points out (*Lancet*, 1929, June 8, p. 1223), is not strictly correct. A two-line reference to the local irritation following the bite of an infected glossina will be found on page 108 of "Manson's Tropical Diseases," ninth edition.

MacRobert (Russell G.). **South American Trypanosomiasis of the Meningo-Encephalomyelitic Type in New York.**—*Jl. Amer. Med. Assoc.* 1929. Jan. 19. Vol. 92. No. 3. pp. 230–231.

Details of a case supposed to be one of South American trypanosomiasis contracted in Venezuela form the substance of this paper.

A woman, aged 36, visited New York from her home in Venezuela in December, 1927, because of failing vision and extreme nervousness. In the right eye there were dustlike and membranous opacities and four retinal exudates below the disk. The fundus was hazy. There were no haemorrhages. The left fundus was normal or slightly pale. In February, 1928, the patient consulted the author with a view to obtaining neurologic examination. No definite signs of organic disease were found, except the following points which at the time seemed unimportant. There were indications denoting heightened irritability of the pyramidal motor system. The deep reflexes were exaggerated and a flexor defense reaction to a stroking of the sole of the foot was rapid and marked. The abdominal reflexes could not be elicited nor could the plantar reflexes. There was no limitation of the temporal fields of vision nor any pallor of the discs.

When next seen two months later, the picture had completely changed. The patient was bedridden and exceedingly ill. She stated that in March a lumbar puncture had been performed and that the spinal fluid was apparently normal. A few days later she developed a temperature of 104° F. with some catarrhal symptoms in the upper respiratory tract. The fever continued in a lesser degree for a couple of weeks and at the end of that time she became noisy, unreasonable, and unmanageable. When seen by the author in April, she lay stretched out stiff in bed and had frequent athetoid spasms of a rigid tonic character, during which she would perspire profusely and moan loudly. She had lost her former ability to speak English and now spoke only Spanish, and this was often unintelligible. She had slight fever, rapid respiration, and a rapid pulse. The palate was immobile. There was a definite Babinski reflex on each side. The pupils reacted to light and accommodation. There was unmistakable evidence of widespread brain involvement and the bulbar symptoms made the condition acutely grave. She continued to have an irregular fever with exacerbations and remissions. The blood count showed a relatively high percentage of lymphocytes, the skin became bronzed, and the patient gave herself up to noisy, meaningless howling. Gradually she became completely quadriplegic, aphasic, and demented.

The author states that the points establishing diagnosis were the long and continuous malaise and remittent fever, the increased percentage of lymphocytes, the high pulse rate, the continuously rapid respirations, the bronzing of the skin, and the widespread brain involvement.

There was a history of a trip by the patient into the interior of Venezuela in September, 1927, at which time it seems probable she was bitten by the germ-carrying fly.

[The case is an interesting one and it is unfortunate that no evidence is produced that it was one of South American trypanosomiasis.]

W. Y.

Niño (Flavio L.). [Jefe de la Sección de Seromicrobiología del Laboratorio Central del Hospital de Clínicas, etc.] Contribución al Estudio de la Enfermedad de Chagas o Tripanosomiasis Americana en la República Argentina. [**Contribution to the Study of Chagas's Disease or American Trypanosomiasis in the Argentine.**]—237 pp. With 8 plates (7 coloured), 9 graphs, 2 maps & 54 figs. 1929. Buenos Aires.

This volume conveys more information than the title would lead one to expect. It is true that it is a "Contribution to the Study of Chagas's

Disease," but it is more than that; from it may be learnt practically all that is known at present concerning the parasite, its vectors, the clinical symptoms to which it may give rise, the pathology of the disease produced, its epidemiology and so on. The information presented is based on eight years' work. The experimental investigations were carried out, first at the laboratory of the Central Military Hospital under Dr. Salvador MAZZA and later at the laboratory of the National Hospital under Dr. MAZZA and Dr. Silvio PARODI.

The vectors exist over a very wide area and there are districts, particularly in the north, where a large percentage of them have in their digestive tract a flagellate which, morphologically and biologically, presents the characters of *Trypanosoma cruzi* and behaves as such experimentally. In the same districts are patients presenting certain symptoms in connexion with the thyroid in particular, which CHAGAS regards as indicative of chronic forms of the disease named after him; such call for study in order that those definitely due to the parasite may be separated from cases of goitre or cretinism of the usual kind. A question naturally arises as to why human cases are comparatively rarely encountered when infected insects are so numerous. The author believes that cases are not after all very uncommon and that a more thorough examination of the people in these districts by house to house visits and the provision of mobile laboratories to facilitate search for the parasite in the blood of man (and animals) will discover a much higher percentage, just as leishmania as a cause of ulcers in America long escaped recognition because it was not specifically looked for.

The work is divided into six chapters. The first, dealing with the history of the disease is very interesting. In 1907, when the Central Railway of Brazil was under construction, the workers found many blood-sucking insects, locally known as "barbeiro," which attacked them at night. Some were caught and dissected and crithidial and leptomonad forms of a flagellate were found in the lower gut. Oswaldo CRUZ inoculated them into guineapigs, marmosets, monkeys, dogs and rabbits, and showed that they were evolutionary forms of a trypanosome differing from those already known and described. Next, examination of the blood of local inhabitants revealed in several of the children a trypanosome which, subsequent experiments showed, behaved like those isolated from the Triatoma. This chapter gives an account of the symptoms in children which need not be recapitulated. Other arthropods were found to harbour the trypanosome; *Triatoma chagasi*, *Rhodnius prolixus*, *Cimex lectularius*, *Ornithodorus* and *Rhipicephalus sanguineus*. Rhodnius was the most diffused vector in Venequeal where Triatoma is absent. In 1915–16 KRAUS and others studied clinical forms of the disease and their relation to endemic goitre and cretinism. He found that in the mountainous zone of the Republic bugs were infected with *T. cruzi* and in parts of this zone were cases of goitre and cretinism, but no *acute* cases of Chagas's disease were met with; also that in the valley of Calcaqué there were infected insects but no goitre, and the same was noted in Buenos Aires and Cordoba. He decided that the chronic form of the disease was difficult to diagnose (parasites may not be found in the blood, but inoculation yields positive results) and was likely to be confused with goitre and cretinism and, finally, that certain points called urgently for solution, in particular: (*a*) whether goitre and cretinism are found in the mountainous districts of Brazil; (*b*) whether absence of Chagas's disease in the Argentine was due to attenuation of the virulence of the trypanosome.

The second chapter records the study of *T. cruzi* in the peripheral blood in infected animals, the morphology in the digestive tract of the vectors and the stages of involution. This is illustrated by some excellent coloured plates. Next follows experimental work on the biology, cultivation and evolution of the parasite and a study of the blood changes resulting from experimental inoculation of animals. Chapter III gives an account of various intermediate hosts. Several species of Triatoma may be infected,

notably *T. megistus* and *T. infestans*, but in seven others the parasite may undergo its evolution. This, of course, is not the same as saying that it does so in nature or that these others are true vectors. *Rhodnius prolixus* and *R. pictipes* are the vectors in Venezuela. Other infectible insects are *C. lectularius*, *C. rotundatus*, *C. boueti*, *Ornithodorus moubata*, and *Rhipicephalus sanguineus*. *T. infestans* is the principal host in the Argentine. CHAGAS and others have found small infecting trypanosomes in the salivary glands and he believes that infection is conveyed by the bite. TORRES has shown that adult insects infect more often than do larvae or nymphs. Experiments are described to demonstrate that infection is not transmitted by the Triatoma hereditarily.

As a general description of the disease Chapter IV is the most important. In it are described the clinical forms, the pathogeny and pathological anatomy, diagnosis, prognosis and treatment. The clinical forms are divided into three groups; acute, with trypanosomes in the peripheral blood; chronic, in which the parasite is not found; thirdly, "Metatrypanoidal" phenomena—goitre, cretinism, infantilism. The chronic group is subdivided into pseudomyxoedematous, myxoedematous, cardiac and nervous forms; and the acute into those with and those without meningo-encephalitis. Yet further subdivisions are made, particularly of the cardiac subgroup according to the character of arrhythmia present. The question of the goitrous form is the subject of a special chapter. "The coincidence of the goitrous zone and that of American trypanosomiasis and the constancy of thyroid enlargement in the children attacked, and the histological findings lead to the conclusion that this is a form of Chagas's disease," says the writer, though many dispute the causative relation.

The idea of attenuation of the virus in the Argentine is based on animal experiment. Guineapigs are very susceptible and rapidly succumb to the Brazilian virus, whereas in the Argentine they were very slightly susceptible. The slow and insidious evolution of the disease in children is adduced as another fact in favour of attenuation; the disease is latent in type, going on for years, the parasite not being found in the blood, although inoculation gives positive results.

This work summarizes all that is known at present on the disease and until fresh evidence is produced will probably be regarded as the standard comprehensive work on a subject of much interest.

H. Harold Scott.

LAUTERBURG (Mark). Erfahrungen mit Tryparsamid bei Schlafkranken. [**Experiences with Tryparsamide in Sleeping Sickness.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1929. May. Vol. 33. No. 5. pp. 251–257. [10 refs.] [Dr. Albert Schweitzer's Hosp., Gabon, French Equatorial Africa.]

The conclusions are :—

1. Tryparsamide proved of the greatest value in the treatment of 29 cases in the second and third stages of sleeping sickness. Even with the severest cases one can reckon on a cure in at least 60 per cent. of instances.

2. Since in about half the patients mild or severe disturbances of vision, even amaurosis, may supervene, the customary doses of 2–3 gm. should be greatly decreased especially in cachectic individuals.

3. Even a relatively small total quantity of tryparsamide (7 gm.) suffices in severe cases to produce a cure. The clinical cure proceeds parallel with the restoration to normal of the number of cells in the spinal fluid.

4. Human infections with *T. rhodesiense*, and also animals infected with trypanosomiasis are resistant to tryparsamide.

5. In general paralysis tryparsamide causes improvement in about half the cases. [The two last conclusions are inferences from the published papers of others.]

W. Y.

BARLOVATZ (A.). L'arsénorésistance dans le traitement de la trypanose humaine par le tryponarsyl (tryparsamide belge). [**Arsenic Resistance in the Treatment of Human Trypanosomiasis by Tryponarsyl.**]—*Bull. Soc. Path. Exot.* 1929. Mar. 13. Vol. 22. No. 3. pp. 201–226.

Details are given of a series of observations on sleeping sickness cases treated by tryponarsyl or tryparsamide. The following are the conclusions :—

1. A small number of cases of sleeping sickness are not benefited by either tryponarsyl or tryparsamide.
2. These patients may be either in the first stage of the disease or in a later stage.
3. When sterilization is not obtained with tryponarsyl or tryparsamide, atoxyl and novarsenobillon likewise fail frequently.
4. This state of arsenic resistance may exist at the time when the patient commences his first treatment. It can quickly develop in patients treated with temporary success by atoxyl or tryponarsyl.
5. Amongst the author's patients it was not possible to incriminate as the cause of the arsenic resistance a previous treatment of insufficient dosage.
6. It is recommended that cases in which arsenicals are not successful should be treated with moranyl or germanin in association with potassium emetic.
7. The last two trypanocidal substances have given good results even in patients with changed cerebro-spinal fluid.

W. Y.

SAUNDERS (G. F. T.). **Report on Cases of Trypanosomiasis treated with Bayer 205.**—*Gold Coast Rep. on Med. & San. Dept. for Year Apr., 1927 to Mar., 1928.* Appendix B. pp. 91–104. [3 refs.]

In a previous report dated February, 1926, three cases were classified as apparently cured ; two of these have since died of sleeping sickness, and the third has relapsed. All the six cases previously reported as improved have died, as also has the case recorded as not improved. The result up to date, therefore, of the treatment of the 16 cases referred to in the previous report is as follows : 13 are dead, one is better but not cured, and two have disappeared. The author remarks that all these cases exhibited at the time of treatment symptoms indicating involvement of the central nervous system, that the majority of cases improved markedly after treatment, and that permanent sterilization of the peripheral blood was produced in all cases but one.

Details are given of 24 further cases all presenting symptoms suggesting involvement of the nervous system and all treated with intravenous injections of Bayer 205. The results to date are as follows :—

Apparently cured	6
Improved	7
Not improved	2
Dead	9

Five similar cases were treated with small doses of very dilute solutions of Bayer 205 intrathecally ; details are given. The author states that alarming symptoms may follow even these small doses, and that advanced cases are not benefited. One acute case with definite cerebral symptoms, but with only 4 cells per cmm. of cerebro-spinal fluid, was apparently cured. An inconclusive attempt was

made to treat a case with trypanosomes suspended in Bayer 205. The immediate result was good, but the patient gradually relapsed, and the condition is now as bad as previously.

W. Y.

MACLEAN (G.). **A Dermatitis associated with "Bayer 205" Treatment of Rhodesian Trypanosomiasis.**—*Ann. Trop. Med. & Parasit.* 1928. Dec. 28. Vol. 22. No. 4. p. 531.

Cases of Rhodesian trypanosomiasis, whilst under treatment with Bayer 205, sometimes develop a well-defined form of dermatitis. The author has seen two such cases, and has heard of two others. In one case, the condition developed two days after the third injection of Bayer 205. It commenced as a papular rash; the papules tended to coalesce. Later, the epidermis darkened and large blisters formed; these became excoriated. After about a week, the lesions began to heal and became dry and scaly. Coincidentally with these skin lesions, there developed conjunctivitis, which became purulent, and stomatitis.

W. Y.

DE ALMEIDA (Eurico). Valor comparativo dos tripanocidas empregados pela zona sanitária do Cuanza. [**Comparative Value of Trypanocides employed in the Cuanza Sanitary Zone.**]—*Bol. da Assist. Méd. aos Indigenas.* Loanda. 1928. Oct. Vol. 2. No. 10. pp. 183–188. French summary p. 189.

The following summary is given :—

1. The prophylactic method adopted, viz.: 10 injections of ·5 gm. of atoxyl given at fifteen-day intervals, and followed by four months rest, gave a negligible number of relapses amongst trypanosomiasis cases in the first period.
2. The attempts at treatment of these in the second, third and last stages of the disease gave only aleatory results; their only chance lay in their segregation into appropriate camps constructed on the Hut-Infirmary plan.
3. It was necessary to try, without interfering with the prophylactic measures, the effect of Bayer 205 in those places where the percentage of infection is greatest, viz.: Zenza, Luinha and Canhoca.
4. A species of trypanosome, differing from *T. gambiense*, was met with fairly frequently in human blood; its identification should be undertaken without delay.
5. The large industrial concerns which manufacture anti-trypanocidal remedies should send to Angola samples of their new products in order that the author and his colleagues might be permitted to collaborate in the great work against sleeping sickness.

W. Y.

PFANNENSTIEL (W.) & SCHARLAU (B.). Heilversuche an trypanosomeninfizierten Tieren auf unspezifischem Wege. Zugleich eine Möglichkeit zur Verbesserung der Germaninwirkung. [**Curative Experiments in Trypanosome Infected Animals with Non-Specific Means. Possibility of improving the Action of Germanin.**]—*Cent. f. Bakt.* I. Abt. Orig. 1929. Vol. 110. Beiheft. No. 6-8. pp. 84*–86*.

The majority of investigators who have interested themselves in the question of the curative effect of human serum on infected mice and

rats have limited their enquiries to a study of the trypanocidal phenomena and have neither concerned themselves with an attempt to analyse the mode of action or to isolate the active substance, nor with the question whether it has any practical value. The work of many authorities suggest that the trypanocidal active substance in human blood is allied to chemotherapeutic drugs; and that these bodies do not act directly on the parasites, but only after incorporation into the animal organism.

The injection of human serum rarely sterilizes infected mice, but after 8 to 14 days a relapse usually occurs, which rapidly leads to death. Repeated injections have progressively less and less effect, and previous treatment of an animal with human serum prevents its therapeutic action when the animal is subsequently infected. These observations indicate that human serum is of little practical therapeutic value and in any case that it would only become so if it were possible to isolate the active substance in pure form.

A series of experiments showed that from the formed elements of the blood no active substance could be prepared, and that this is to be found only in the fluid portion of the blood. The authors' efforts to isolate the active principle are not yet completed, but they seem to indicate the direction which investigations might take, viz., by concentration of the serum to increase its activity. Normal human serum was dried in a Faust-Heims apparatus, pulverized in an agate mortar, and taken up in a quantity of physiological saline. By this means a fluid was obtained through which—provided it had above a certain serum powder concentration—it was found possible by a single subcutaneous injection of 0·3 cc. definitely to cure a heavily infected dourine mouse.

These experiments showed that by this technique smaller amounts of serum powder sufficed than did a corresponding amount in the serum itself. An injection of 0·3 cc. serum (containing about 25 mgm. of dry substance) was always followed by a relapse in 8 to 14 days, whereas an injection of the serum powder solution prepared from the same amount of serum resulted in permanent cure.

This led the authors to enquire whether the action of germanin might not be strengthened if it were combined with dry serum. This proved to be the case, as by simultaneous intraperitoneal injections of inactive doses of germanin and dry serum, infected mice were permanently cured. Similarly, the action of neosalvarsan was increased, but to a less extent than that of germanin.

The authors are at present engaged in an attempt to obtain the trypanocidal active substance of human serum in such a degree of purity that it may be possible to cure larger animals with it. Preliminary experiments on macaques appear to be hopeful.

W. Y.

ZAVAGLI (Vittorio). Note di bacterioterapia e di chemioterapia nella infezione sperimentale da *Trypanosoma brucei*. [**Bacteriotherapy and Chemotherapy in Experimental Infection with** *Trypanosoma brucei*.]—*Arch. Ital. Sci. Med. Colon.* 1929. Jan. 1. Vol. 10. No. 1. pp. 14–29. English summary p. 30. [Pasteur Inst., Paris.]

This article is of interest in adducing further evidence of the antagonism of two infections, one protozoal, the other bacterial.

White mice were inoculated with known numbers of *Trypanosoma brucei* and with various bacterial vaccines— staphylococci, streptococci, pneumococci, meningococci, *B. pyocyaneus*, and Pasteur's anthrax vaccine 1 and 2. The five first-named had no effect on the evolution of the trypanosomes in the mouse, but with the Pasteur "Premier vaccin" the trypanosomes were late in appearing and the animals survived, whereas with either separately death occurred from the infection.

The action of injected chemical substances on the development of trypanosomes was not great in non-toxic doses. The double thiosulphate of Au and Na in a dose of 3·5 mgm. subcutaneously was toxic without destroying the trypanosomes, but 0·1 to 0·3 mgm. delayed their appearance; colloidal magnesium hydrate had a similar, if anything a rather more definite effect. A large number of chemical substances was tested, but these were the only ones to give any definite result.

H. Harold Scott.

KRITSCHEWSKI (I. L.) & KAGANOVA (S. S.). Zur Frage der antimutativen Wirkung des Germanins. [**The Question of the Antimutative Action of Germanin.**]—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1929. Vol. 61. No. 5/6. pp. 478–485. [2 refs.] [Microb. Research Inst., Education Commissariat R.S.F.S.R., Moscow.]

Shortly before his death MORGENROTH published the important observation that germanin possessed the power of suppressing the relapse strain formation of trypanosome races (*T. brucei* strain Prowazek). This was called the "antimutative" capacity of the drug. [See this *Bulletin*, Vol. 21, p. 757.]

One of the authors, working with another strain of *T. brucei* (Berlin), failed to confirm MORGENROTH'S observation, and with a view to clearing up the discrepancy and to ascertaining whether it was due to the particular parasite with which he was working, the authors repeated the experiments with 8 different strains and species of trypanosomes.

The conclusions are as follows :—

1. The antimutative action of germanin on trypanosomes is not unconditional; it exerts itself only in higher or less degree according to the species and strains of the trypanosomes.
2. The antimutative action of germanin is strongest with *T. brucei* strain Prowazek, less with *T. equiperdum*, and quite slight with *T. pecaudi* and *T. evansi*.
3. With *T. brucei* Berlin, *T. brucei* Paris, *T. sauru* and *T. rhodesiense*, germanin exhibits no antimutative power.

W. Y.

HORNBY (H. E.). **The Detection, by Means of the van den Bergh Reaction, of Incipient Liver-Necrosis due to Antimony Therapy.**—*Vet. Rec.* 1928. Aug. 11. Vol. 8. No. 32. pp. 648–653. [4 refs.] [Dept. Pharmacol., Univ. College, London.]

The author states that up to the present nothing has superseded tartar emetic in the treatment of the common forms of African bovine trypanosomiasis. The great drawback to its use is the danger of acute liver necrosis. In order that antimony therapy might be rendered

safe, it appeared necessary to find a simple liver function test which would reveal the effect on that organ of previous injections and divulge with what safety the next could be given. With this object in view, the author performed the van den Bergh test on rabbits dosed experimentally with tartar emetic. The following summary of the work is given :—

" The chief drawback to the use of tartar emetic as a trypanocide is that it may cause acute liver necrosis.

" Ordinarily, liver necrosis is the result of a series of doses ; and this research had as its objective the finding of a simple liver-function test which would reveal the effect on that organ of previous injections, and divulge with what safety the next could be given.

" It was thought that the van den Bergh test of bile-pigments in serum or plasma might fulfil these conditions. A description of the test is given.

" Using initially healthy rabbits it was possible to produce various degrees of liver injury by means of intravenous injections of tartar emetic, and to correlate the lesions with plasma reactions to the van den Bergh test.

" When a series of medicinal doses of tartar emetic are given, the injection which causes fatal necrosis is generally preceded by one which occasions only slight necrosis, and it is for the detection of this early injury that the van den Bergh test is particularly valuable.

" Damage to liver cells amounting to acute fatty degeneration, but short of actual necrosis, may not provoke a van den Bergh reaction. Nevertheless, the rule is that if an injection is *not* followed by a van den Bergh reaction, it is safe to repeat the dose.

" Reversely, if an injection sets up a reaction then it is unsafe to repeat the dose until the reaction has subsided completely.

" It is recommended that in tartar emetic therapy one should start with the small dose that experience has taught is safe, and use the van den Bergh test while raising the dose to the desired medicinal one and to the end of treatment.

" Fouchet's test is described. It is a good and delicate confirmatory test of the presence of bile pigment in serum or plasma."

W. Y.

PHILIPTSCHENKO (A.). Zur Frage über den Entwicklungszyklus von Trypanosomen im Säugetierorganismus. Vorläufige Mitteilung. [**The Developmental Cycle of Trypanosomes in the Mammalian Host.**]—*Cent. f. Bakt.* I. Abt. Orig. 1929. Feb. 16. Vol. 111. No. 1/3. pp. 125–138. With 6 text figs. [Pasteur Bact. Inst., Leningrad.]

The author emphasizes the fact that the mechanism of the production of relapses which are so common in some protozoal and spirochaetal infections is not thoroughly understood. Most workers have confined their attention to the part played by the host and have ignored to a great extent the parasitic factor. It is known that certain protozoa renew, from time to time, their organism by a reconstruction of their nuclear apparatus (endomixis).

Certain strains of malaria parasites and of pathogenic trypanosomes have been preserved for many years in vertebrate hosts without having been able to pass through their sexual cycle. This fact could be explained either by the immortality of the protozoa (WEISSMANN) or by the hypothesis that under certain circumstances complicated biological renewal processes of their organism take place. The latter possibility appears to the author as the most likely and it is with this question that the present paper is concerned.

The experiments were performed with guineapigs, rabbits and mice and the laboratory strain of nagana (Yakimoff). The inoculations were so arranged that approximately the same number of parasites was injected subcutaneously on each occasion. The number of parasites in the peripheral blood of the inoculated animals was determined as far as possible every day at the same hour. At first they were counted against the red cells in a Thoma-Zeiss apparatus, but later the simple course was followed of counting the parasites in a number of microscope fields (Oil immersion and Oc. 4) and then calculating the number present in 100 fields. In addition, in the case of some of the guineapigs, daily observations were made on the temperature, weight and blood picture (erythrocyte and leucocyte number, haemoglobin value, and differential leucocyte count). Some of the animals died a natural death and others were killed by chloroform at various periods during the infection; in both cases smears were made from most of the organs and the organs themselves were examined histologically.

The experimental infection in the guineapig assumed one of two forms—the acute form or the subacute-relapse form. In the former the disease lasted 8–15 days and in the latter 18–35 days. The incubation period varied from 2 to 12 days and appeared to be somewhat greater in the subacute cases than in the acute. No definite differences were made out in regard to the temperature and weight curves or the red cell count; both types of infection were characterized by a constant decrease in the number of erythrocytes and in the haemoglobin value. This, however, did not hold true for the leucocytes: in the first stages of the disease there was almost always a moderate leucocytosis which was followed by a fall in number. In the acute cases this fall was continuous and in direct relationship to the increasing number of trypanosomes; in the subacute cases the period of disappearance or decrease in the number of trypanosomes was marked by an increase in the number of leucocytes and, conversely, when the trypanosomes again increased in number the leucocytes decreased.

The two types of infection are most clearly distinguished by the behaviour of the trypanosomes in the peripheral blood. In the acute form the number of parasites increases incessantly day by day; in the subacute forms the trypanosome curve shows two peaks clearly separated by a marked depression, which may even amount to a total disappearance of parasites from the blood. In both forms death occurs under similar conditions, and post-mortem examination shows no definite differences. If, however, the animal is killed at the time of disappearance of the parasites a number of appearances are observed which deviate from those discovered in animals in which the disease has run its course. Above all, in such cases the customary changes were much less pronounced. The lymph glands were but slightly enlarged and hyperaemic, and hyperaemia and haemorrhages from the intestine and diaphragm were absent. In these cases, however, there were almost invariably small fresh haemorrhages into the lung tissue; an appearance which was never seen in other cases.

In the author's series of experimentally infected guineapigs acute and subacute infections appeared quite irregularly; and acute infection might be followed by two or three subacute infections or *vice versa*. Careful study of the protocols, however, suggested that possibly the stage of the infection at which blood was withdrawn for inoculating the next animal might determine the matter. It was eventually found that if the subinoculation was made from blood withdrawn early in the infection a subacute infection might be expected, whereas if it were made from blood taken at a late stage an acute infection

would result. If in a series of animals inoculations were made always with trypanosomes withdrawn at the end of the infection, it was found that one relapse type of infection always followed two, or at the most three, acute infections; under these conditions of experiments two or more subacute infections never followed one after the other. This alternation of both types of infection the author calls the normal progress type of the artificial trypanosome disease in guineapigs. Each repetition of two or more relapse forms one after the other is a departure from the normal type and is dependent entirely on the time at which the blood was taken for inoculation. In the normal progress type of the artificial trypanosome disease the whole series of generations from one relapse to another must be regarded as a single developmental cycle of the parasites within the guineapig.

The author next passes to a consideration of the morphology of the trypanosomes in the acute and subacute types of infection. In the majority of cases nothing of special significance was found, but in isolated cases of the relapse type just at the beginning of the increase in parasites a few examples of the so-called "chromidial forms" were discovered. These are distinguished from the normal forms by their feebly staining cytoplasm and especially by the absence of a nucleus which is distributed as a chain of chromatin granules. Such forms are exceedingly rare and found only in the first stage of the relapse period. In some cases striking differences in the number of divisional forms and in the type of division were observed before the disappearance of the trypanosomes and after their reappearance during the relapse. In the former case, practically only binary division is seen, whilst in the relapse forms undergoing multiple division are encountered.

In examining smears and sections of the organs nothing of special interest was discovered, except in those of the lungs of animals killed at the time of disappearance of trypanosomes from the blood. In the regions showing the small haemorrhages, an occasional small round sharply-defined mass 12 to 20μ in diameter was seen in the alveolar wall. On suitable staining this was found to consist of a thin capsule containing a great number of bodies, 2 to 3μ in diameter, which resembled merozoites and consisted of a nucleus and cytoplasm. In some preparations a darkly stained rod was seen close to the nucleus, reminding one of Leishmania.

As a result of his observations, the author believes that relapses are due primarily to a biological property of the parasites and not to immune processes of the organism of the host, and that the bodies he has discovered in the lungs represent a reconstruction process of the nuclear apparatus of the parasite.

W. Y.

SOLLAZZO (Germano). Der Einfluss des Hungers und der Avitaminosen auf die Resistenz gegen Trypanosomen-Infektionen. [**The Influence of Starvation and Lack of Vitamins on the Resistance against Trypanosome Infections.**]—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1929. Vol. 60. No. 3/4. pp. 239–246. [17 refs.] ["Robert Koch" Inst. for Infectious Diseases, Berlin.]

Reference is made to previous work showing that starvation and vitamin deficiency reduced the body's resistance to bacterial infections; hitherto, however, no observations have been made on the influence of these factors on protozoal infections.

In this work, the author has examined the effect of starvation and lack of vitamins in pigeons inoculated with *T. brucei*. He first showed that pigeons normally are completely refractory to *T. brucei*, and that when large amounts of a highly virulent strain are injected, the parasites quickly disappear from the circulatory blood and internal organs. Pigeon serum mixed with *T. brucei* and then injected into mice does not prevent infection. Pigeons were subjected to complete starvation and given only water. Others were fed exclusively on white corn from which the antineuritic vitamin had been removed: these animals began to develop symptoms after 16 to 32 days, polyneuritis reached its height after 20 to 35 days, and death occurred in 28 to 70 days.

The experiments performed with the normal animals, with those in a state of starvation, and with those deprived of antineuritic vitamin are described in detail. The conclusions reached are as follows :—

Experiments to infect normal pigeons with nagana trypanosomes have shown that the birds are insusceptible, and that the parasites are unable to multiply in the body of the bird. Of 10 pigeons only two showed a blood infection during the first 24 hours and this had disappeared within 48 hours.

In normal pigeons there is no focus or development of the parasites in the internal organs.

In the starving animals 5 out of 6 exhibited a decrease of resistance to the trypanosomes: in two animals there was an obvious multiplication of the parasites in the peripheral blood, and in 5 of the 6 the inoculation was positive; in one case parasites were proved by inoculation to be present in the blood up to the fifth day.

Deficiency of vitamin B rendered possible the multiplication of the trypanosomes in the body of the pigeon, so that in one case they were demonstrated up to the eleventh day by subinoculation. It is possible that the trypanosomes had a feeble pathogenic action which expressed itself in an acceleration of death due to lack of vitamin B.

W. Y.

KLIGLER (I. J.) & COMAROFF (R.). **Susceptibility and Resistance to Trypanosome Infections. V. The Resistance of Rats to Infection.** —*Ann. Trop. Med. & Parasit.* 1929. Apr. 26. Vol. 23. No. 1. pp. 103–120. With 2 figs. [11 refs.] [Dept. of Hyg., Hebrew Univ., Jerusalem.]

The following summary is given :—

"A study was made of the course of a trypanosome infection in rats and of the character of their resistance to such infections. The investigation was carried out by following the course of infection in rats by repeated counts of the number of trypanosomes in the circulation. An analysis of the data indicates that :—

"1. The infection in the rat is of an order intermediate between that in the mouse and guineapig. The rat possesses a resistance which is probably the same in kind as, but different in degree from, that of the guineapig.

"2. Although the infection is a progressive one there is a constant destruction of trypanosomes throughout the course of infection.

"3. Depression of the resistance may result in an infection which approximates more closely that of the mouse. This phase of the question is now under investigation.

"4. At time of death the concentration of trypanosomes in the circulation is constant. For the species studied, the average numbers were 1,440,000 for *T. evansi*, and 1,420,000 for *T. gambiense*. The red cell count is also greatly reduced, but varies a great deal more than the trypanosome count.

"The direct causal relation of these factors to death of the animals is not certain. It appears, however, that death is due to injury produced by the metabolic products of the trypanosomes (lactic acid) and that the organisms must reach a certain concentration, which differs with different species, before they can affect the changes or intoxication which lead to death. Disturbance in the oxidation mechanism is probably a critical element in the process."

W. Y.

ADAMS (Paul). Ueber das Wesen der trypanoziden Wirkung menschlichen Normalserums. [**The Trypanocidal Action of Normal Human Serum.**]—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1928. Vol. 58. No. 5/6. pp. 459–482. [41 refs.] [Hyg. Inst., Westphalian Wilhelms Univ., Münster.]

After summarizing the observations of previous workers, the author points out that the mechanism of the trypanocidal action of normal human serum is still by no means clear. The questions which the author has attempted to answer in this paper are first, whether other substances, which can be regarded as "irritant bodies," can develop in infected mice a trypanocidal action similar to that of human serum; and second, what properties render the human serum trypanocidal.

White mice infected with nagana (strain 30 Teichmann–Braun) or dourine were used exclusively in these experiments. About 0·2 cc. of blood from heavily infected mice, diluted in saline and injected subcutaneously, produced in the experimental animals a very acute infection. In the case of the nagana strain the parasites were numerous in the blood in 50–60 hours and death occurred in the majority of instances in 3 days. With the dourine strain the trypanosomes appeared in the blood on the third day and death as a rule took place on the fourth and fifth day. The injection of the sera or other substance was generally made subcutaneously, but sometimes intravenously or intracutaneously.

The following summary of the experiments and conclusions is given :—

1. The trypanocidal effect of the injection of normal human serum in trypanosome infected mice is not due to a purely "irritant body" action. In comparable experiments it was found that injections of such substances as Aolan, Kaseosan and Yatren-kasein, were without any effect on the trypanosome infections in mice. Similarly the injection of other substances such as bile, urea, emetine, iodine, weak acids, etc., which on injection into rabbits cause an increase in the anti-typhoid action of the serum, failed to cause the disappearance of trypanosomes from the blood of mice

2. The sera of rabbits, guineapigs, sheep, cattle, horses, pigs, and the lower monkeys (macaques) were likewise without action, as was also the serum of horses which had been immunized against diphtheria.

3. Macaques could be fatally infected with the nagana strain.

4. In contrast to the action of germanin that of normal serum did not in the author's experiments result in complete sterilization of the infection; about 7 days after the injection of the serum a relapse occurred. Further injections caused the parasites to disappear again for some days, but the effect of repeated injections gradually became weaker.

5. The trypanocidal power of human serum is definitely diminished by heating to 56° C. Serum inactivated at 56° C.–60° C. has a very poor trypanocidal action as compared with that of active serum. Heating for half an hour at 62° C. completely destroys the trypanocidal power of normal human serum.

6. The trypanocidal power is also lessened by keeping the serum for from 2–4 weeks at room temperature.

7. Serum inactivated by heat cannot be re-activated by the addition of fresh guineapig complement. A certain reactivation of old serum through the addition of fresh guineapig serum was observed in one case, but the observation could not be repeated.

8. Human blood which had clotted slowly at 0° C. furnished a weaker trypanocidal serum than that which had clotted quickly at 37° C. The different degree of the destruction of blood platelets consequently appears to be not without significance.

9. Syphilitic sera, giving a positive Wassermann reaction, is, in general, more strongly trypanocidal than Wassermann-negative sera. In one case a mouse was completely cured of a nagana infection by a single injection of a Wassermann-positive serum. The stronger action of the Wassermann-positive serum is also seen after inactivation at 56° C. for half an hour.

10. The trypanocidal action of human serum is of a specific nature and can apparently be increased through syphilitic infection.

W. Y.

HELM (R.). Zur Aetiologie des Oedems bei der Trypanosomiasis der Tiere. [**On the Etiology of the Oedemas in the Trypanosomiasis of Animals.**]—*Cent. f. Bakt.* I. Abt. Orig. 1929. Vol. 110. Beiheft. No. 6/8. pp. 87*–89*.

Reference is made to the work of BATTAGLIA who states that the oedema in trypanosomiasis is in large part due to marked degenerate and atrophic lesions in the thyroid and parathyroid glands [this *Bulletin*, Vol. 24, p. 972]. The author then records observations, made by him before the war, which he considers throw further light on the mechanism of this symptom. Oedema may manifest itself at any time in the disease—sometimes it is seen after a few days, but more often shortly before the death of the animal. He recalls the case of a horse which had extensive oedema all over the under part of its belly ; the owner stated that it had been in a tsetse region for weeks previously. Blood examination was negative and remained so for four days. After the lapse of these four days there set in a thrombosis of the left femoral artery and a complete palsy of the hind limb. Fibrolysin 11·5 cc. was injected into the jugular vein. After an hour the swelling had definitely decreased and numerous trypanosomes appeared in the blood. The following day the swelling had completely disappeared and the palsy likewise.

This observation induced the author to institute an enquiry whether the administration of fibrolysin in a trypanosome-free period caused the re-appearance of parasites in the peripheral blood. He conducted experiments with one horse, one dog, ten rabbits and ten guineapigs injected with nagana or dourine. Unfortunately, both the horse and the dog were failures as neither showed oedema or trypanosome-free intervals. Very satisfactory observations were, however, made with seven of the rabbits. In every case with a single exception an injection of 1·15 cc. of fibrolysin in a trypanosome-free period sufficed to cause the appearance of parasites in the peripheral blood, as a rule, within 15 minutes.

The author now explains the origin of the oedema in the case of the horse above described on the hypothesis that probably an agglomeration of trypanosomes with other blood elements had taken place. The thrombus and its constituent parts were set free by the thrombolysin and thus trypanosomes reappeared in the peripheral blood.

W. Y.

KLIGLER (I. J.) & GEIGER (A.). **Lactic Acid Content of Blood of Trypanosome Infected Rats.**—*Proc. Soc. Experim. Biol. & Med.* 1928. Dec. Vol. 26. No. 3. pp. 229–230. [2 refs.] [Dept. of Hyg., Hebrew Univ., Jerusalem.]

The authors point out that experimental trypanosome infection in rats presents one of the simplest pictures of protozoal blood infection. The significant features of the infection are: (1) An increase of the trypanosomes to a constant number which seems to be characteristic of the species; (2) Anaemia, which is variable, ranging between 30 per cent. and 50 per cent. of the original cell count; (3) Sudden death with symptoms of dyspnoea within 10 to 36 hours after the trypanosomes have reached the maximum concentration. There are no toxic symptoms and the injection of large numbers of trypanosomes or of a large amount of serum taken from an animal shortly before death does not produce any symptoms of intoxication.

These facts give rise to two questions, firstly, the reason for the cessation of multiplication of the trypanosomes; and secondly, the actual cause of death.

With a view to answering these questions, the authors decided to study the changes in the blood chemistry during the course of the infection. SCHERN (1926) has shown that there is a reduction in the fermentable substances in the liver of trypanosome infected animals, and consequently it seemed likely that during the infection the available glycogen and glucose reserve was used up by the trypanosomes to the point of exhaustion, and that at the same time lactic acid was produced which caused progressive exhaustion of the alkali reserve, this depletion ultimately resulting in the death of the animal. In a table the concentration of lactic acid in trypanosome infected rats at different stages of the infection is shown. From this table it appears that there is a progressive rise of the lactic acid concentration in the blood, which runs parallel with the increase in the number of trypanosomes in the blood stream.

W. Y.

MORISHITA (Kaoru). [**Flagellate Parasite of** *Triatoma rubrofasciata* **(Hemiptera Heteroptera) and the Trypanosoma developing from it in Laboratory Animals. (Preliminary Note.)**]—*Taiwan Igakkai Zasshi* (*Jl. Med. Assoc. Formosa.*) 1928. Dec. No. 285. [In Japanese. English summary pp. 77–78.] [Govt. Research Inst., Formosa, Japan.]

It is well known in Formosa that the reduviid bug *Triatoma rubrofasciata* is prone to attack man and cause more or less severe symptoms. The bugs captured in houses harbour flagellates in their intestines; 100 per cent. of the females and 78·5 per cent. of the males are infected. The flagellates were never found in the body cavity nor in the salivary glands or malpighian tubes. In the intestines various stages were found, viz.: long and short crithidia, leishmania forms, metacyclic trypanosomes and various transitional forms.

The presence of metacyclic trypanosomes suggested that the parasite was a trypanosome of a vertebrate host. Intraperitoneal inoculation of the intestinal contents of the bugs into mice produced infection in 5 of 6 cases; subcutaneous inoculation failed. The incubation period varied from one to eight days: the parasites in the peripheral blood were always scanty and were to be seen for only 7 to 37 days.

Dividing forms were occasionally encountered. In a splenectomized mouse the trypanosomes were found in the blood for as long as 63 days. The passage through mice succeeded for only two generations. The infection in mice was apparently not pathogenic.

In the blood of the mouse the parasite is very long and slender, measuring on an average 56·9μ in length and 3·1μ in breadth. The ratio of the distance between the blepharoplast and the posterior end of the body to the total length of the body is 1 to 2·7. The parasite was never found in the tissues or organs of the mouse. It develops in the condensation fluid of blood agar.

W. Y.

JOHNSON (Thurston L.). **In Vivo Trypanolysis with Especial Reference to Zones of Inhibition, Relapse Phenomena and Immunological Specificity.**—*Amer. Jl. Hyg.* 1929. Mar. Vol. 9. No. 2. pp. 260–282. [39 refs.] [Dept. of Hyg. & Bact., Univ., Chicago.]

The following are the conclusions :—

" (1) If mice are infected with *T. equinum*, *T. brucei* or *T. equiperdum* and treated with the proper doses of trypanolytic serum, they show a sharp trypanolytic crisis and a prolongation of life as compared with untreated controls.

" (2) When a series of mice, infected with *T. equinum* or *T. brucei*, are given graded doses of immune serum, doses greater than the minimal effective dose are not necessarily effective, but zones of effectiveness may alternate with zones of non-effectiveness (zonal phenomenon).

" (3) The occurrence of the zonal phenomenon is dependent upon the number of trypanosomes present in the blood at the time of the administration of immune serum. Thus the following relationship is found in strain J4 of *T. equinum*.

Number of trypanosomes per standard microscopic field at time of treatment with immune serum.	Occurrence of the zone phenomenon.
1 to 5	No zone phenomenon. All doses greater than the minimal effective dose are effective.
9 to 33	Zone phenomenon. Doses greater than minimal effective dose show alternate zones of effectiveness and non-effectiveness.
45 to 50	No lysis in any dose.

Similar results have been obtained with a strain of *T. brucei*.

" (4) A study of relapsing strains arising after serum treatment in mice has yielded the following results :

"(*a*) There is a great variability in the resistance acquired by the trypanosomes after *in vivo* contact with immune serum. Thus, if a series of infected mice is treated with immune serum and lysis occurs, and again treated with the same serum when the relapse strain has reached the same blood population as before, a second lytic action occurs in a small number of cases contrary to the general preconceived ideas.

" (*b*) In those relapse strains which did not become resistant, there is a change in the relationship of the number of organisms per cmm. and the occurrence of zones of inhibition. Thus J4 which originally gave the zone phenomenon when there were from 10 to 30 trypanosomes per standard field, after relapse, gave zones of inhibition when there were only 1 to 3 parasites per field.

"(5) The action of the lytic antibody is as definite on heterologous strains as on the homologous strain. This is not in agreement with previous reports of the extreme sensitivity of cross-immunity tests.

"(6) Some permanent cures have been obtained. It is of interest to note that of six obtained, five resulted from the action of heterologous serum in one experiment."

W. Y.

JOHNSON (Thurston L.). **The Non-Occurrence of the Zone Phenomenon in the Curative Action of Drugs and Normal Human Serum in** *Trypanosoma equinum* **Infection.**—*Amer. Jl. Hyg.* 1929. Mar. Vol. 9. No. 2. pp. 283–291. [3 refs.] [Med. Dept., Univ. of Arkansas, Fayetteville.]

The following are the conclusions :—

"Zones of effectiveness and non-effectiveness of immune serum *in vivo* analogous to the Neisser-Wechsberg phenomenon *in vitro* have been previously described in mice infected with *T. equinum*. The present work involving 16 series containing a total of 280 mice would seem to indicate that a similar phenomenon does not occur when a series of infected mice are treated with graded doses of several of the trypanolytic drugs, but that all doses above the minimal effective dose destroy the trypanosomes. Likewise, from a study of 5 series involving a total of 75 mice, all doses of normal human serum above the minimal trypanocidal dose destroy the trypanosomes."

W. Y.

SCHILLING (Claus) & SOLLAZZO (Germano). Wirken Trypanosomen, mit Immunserum behandelt, als Antigen ? [**Do Trypanosomes treated with Immune Serum act as Antigen ?**]—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1929. Vol. 59. No. 3/4. pp. 219–221. [3 refs.]

The authors point out that as yet little is known regarding the mode of action of immune sera against trypanosomes. They observed that a mouse which had been injected with a mixture of guineapig immune serum + *T. brucei* (strain Prowazek) remained trypanosome free for 20 days, and even after a second large injection of trypanosomes remained free from parasites for several days and did not die until the seventh day, although the control animals certainly die in 3 to 4 days. The author next inquired whether this increased resistance was a constant phenomenon. They employed a dried immune rabbit serum, the activity of which kept well ; it was not parasiticidal *in vitro* as even after 24 hours the parasites were still motile. Trypanosomes kept in fresh immune serum are certainly killed. Experiments showed that the protective action was always marked when the serum-trypanosome mixture was injected into rats or mice ; but that an immunity against a large injection of trypanosomes, even after several repeated treatments, was only to be seen in quite small degree. Similarly, the serum of a rat, which had received three trypanosome+ immune serum injections and had remained free from infection, when mixed with trypanosomes and injected into three mice, only prolonged life for 2 to 4 days.

In further experiments trypanosome blood was mixed with immune serum and fresh guineapig serum (complement) and allowed to stand at 37° C. for 1 hour : the mixture was then centrifuged and the deposit

injected into mice. In controls the whole mixture was injected. In both cases infection, although delayed, occurred, from which it is concluded that the addition of complement is without significance.

The conclusions are :—

1. Immune serum exerts at times a parasiticidal action against trypanosomes *in vitro*, from which a direct action in the animal body can be inferred. Sometimes, however, it does not kill the parasites *in vitro*, but when injected with the trypanosomes into an animal prevents infection.
2. The latter action is not dependent on the complement content of the animal body.
3. The combination between immune-body, complement and trypanosomes could not be demonstrated with the nagana strain used.
4. An immuno-antigen action of the trypanosome suspension in immune serum did not emerge, or only in an indefinite manner, in these experiments.

W. Y.

SCHILLING (Claus). Ueber Immunität bei Trypanosomeninfektionen. [**On Immunity in Trypanosome Infections.**]—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1929. Vol. 61. No. 5/6. pp. 381–383. [" Robert Koch " Inst., Berlin.]

A parafuchsin resistant strain was produced by treatment of animals infected with a strain of nagana (Prowazek) ; this strain was blepharoplastless. With this strain 8 rats were infected and two days later treated with 0·5 cc. of a 1 in 1,000 solution of tartar emetic. Five days later, 4 were injected with the original Prowazek strain and 4 with a strain of nagana which had been maintained for years in Hamburg.

The following conclusions are reached from these experiments :—

1. If an infection due to a chemically changed strain is completely cured, or reduced to a labile infection, and if later the original strain is superinjected, infection does not result. The specific antigen property of the strain is not influenced by chemical action (drug resistance, loss of blepharoplast).
2. The labile infection with a (chemically changed) laboratory nagana strain confers no immunity against a laboratory nagana strain of different origin.
3. Infections with two different strains can run concurrently without influencing or adding to each other's action.

W. Y.

REGENDANZ (P.). Der Blutzucker bei Trypanosomeninfektionen. [**The Blood Sugar in Trypanosomal Infections.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1929. May. Vol. 33. No. 5. pp. 242–251. [10 refs.] [Inst. for Ship & Trop. Diseases, Hamburg.]

The behaviour of the blood sugar in trypanosomal infections of animals has attracted a good deal of attention during recent years ; but the results obtained by various workers have been by no means uniform. The author has accordingly conducted further experiments on the subject and has reached the following conclusions :—

1. The blood sugar value, in the case of rats infected with pathogenic trypanosomes, is depressed only at the end of the disease.

2. Infections of monkeys with *T. rhodesiense* are accompanied by a decrease of blood sugar, but this is independent of the number of trypanosomes in the blood.

3. In monkeys infected with *T. rhodesiense* the decreased blood sugar is restored to normal by an injection of suprarenalin.

4. The liver of a monkey, which has died as the result of infection with *T. rhodesiense*, contains glycogen in great amount, so that the diminution in blood sugar cannot be due to lack of sugar-forming substances.

5. The disturbance of sugar metabolism is much more readily explicable on the toxic action of the trypanosomes on the organs of importance for sugar metabolism.

W. Y.

SCHERN (Kurt). Zur Trypanosomenarbeit von Regendanz und Tropp. [**On the Trypanosome Work of Regendanz and Tropp.**]—*Cent. f. Bakt.* I. Abt. Orig. 1929. Feb. 16. Vol. 111. No. 1/3. pp. 139–143.

REGENDANZ (P.). Erwiderung auf den Artikel von Schern: "Zur Trypanosomenarbeit von Regendanz und Tropp," Bd. 111, S.139 dieser Zeitschrift. [**Reply to the Article of Schern.**]—*Ibid.* 1929. May 28. Vol. 112. No. 3/4. pp. 319–320. [1 ref.]

These papers are polemical and are apparently the result of the article by REGENDANZ and TROPP (this *Bulletin*, Vol. 24, p. 971), who hold that death in rats infected with trypanosomes is due to the action of toxins. After discussing the matter in considerable detail, Schern concludes that his own work and that which has followed it have provided proof that disturbance of sugar metabolism is a decisive factor in the pathogenesis of trypanosomiasis and spirochaetosis.

W. Y.

DE ALMEIDA (Eurico). A reacção de Maki Takata-Kiyoshi-Ara e os graus de positividade no segundo periodo da doença do sono. [**The Takata-Ara Reaction in the Second Stage of Sleeping Sickness.**]—*Bol. da Assist. Méd. aos Indigenas.* Loanda. 1928. Dec. Vol. 2. No. 12. pp. 309–329. French summary p. 329.

The Takata-Ara test is a flocculation reaction obtained by adding to 1 cc. of cerebrospinal fluid one drop of sodium carbonate (10 per cent. solution) and 0·3 cc. of a freshly prepared mixture consisting in equal parts of 0·5 per cent. solution of corrosive sublimate and 0·02 per cent. fuchsin. The result is generally positive in nervous forms of syphilis and in acute meningitis. In this article the author records his results in 19 untreated cases of sleeping sickness in the stage of somnolence and tremor, and in 47 patients presenting the same symptoms but undergoing treatment.

Brief details of each case are given and the results may be summarized by saying that in the untreated the reaction is positive and occurs usually within three minutes, whereas in the treated the reaction is delayed up to half an hour and in some instances may be negative after 24 hours. The test is regarded therefore as a diagnostic aid in cases in the bush or in a district out of reach of laboratory investigations.

H. Harold Scott.

GALLIARD (H.). De quelques causes influant sur l'évolution de l'infection mixte à trypanosomes et à tréponèmes. [**Causes influencing the Development of Mixed Infection with Trypanosomes and Treponemes.**]—*Ann. Parasit. Humaine et Comparée.* 1929. Jan. 1. Vol. 7. No. 1. pp. 57–60. [5 refs.] [Parasit. Lab., Faculty of Med., Paris.]

In this work the author used *Trypanosoma brucei* (strain Mesnil) and various spirochaetes, e.g., *Treponema duttoni, T. hispanicum* and especially *T. crocidurae,* which gives mixed infections of very long duration.

He has studied what causes are able to influence the evolution of a mixed infection in the mouse and rat. The inoculation, at the chronic period of infection, of spirochaetes or of various sera, has no influence on the course of the disease, with the exception that the inoculation of trypanosomes obtained at the terminal period of a mixed infection leads quickly to death.

On the contrary, the evolution of the disease is expedited and death follows quickly if the mixed virus is inoculated into animals not absolutely new. Such are mice and rats prepared by the injections of serum (especially human serum) or cured a long time previously of spirochaetal infection and no longer immune. Animals, at the commencement of a spirochaetosis, succumb rapidly on inoculation of the virus. The same applies for rats and mice infected with *Trypanosoma cruzi* and especially in the case of rats cured, or infected with, *T. lewisi.*

It is not possible to explain in all cases the rapidity of the evolution by a diminution of the resistance of the host or by enfeeblement of the organism, since one frequently sees the animals die of cachexia, of acute spirochaetosis or as the result of repeated haemorrhages, without ever in these cases being able to attribute death to trypanosomiasis.

All that one can say is that trypanosomes and spirochaetes in the course of a mixed infection have lost their individuality, have acquired certain peculiar properties, and form an association in a state of unstable equilibrium. The equilibrium is broken if the virus is inoculated into an individual presenting any modification whatever of the reactions of the organism—modifications which do not lead to any alteration of the leucocyte formula—without there being necessarily any lessening of its resistance.

W. Y.

PEDRAZZI (Arrigo). Influenza delle spirochetosi ricorrenti sullo sviluppo di alcune tripanosomiasi. [**Influence of Relapsing Fever on the Development of Certain Trypanosomiases.**]—*Arch. Ital. Sci. Med. Colon.* 1929. Feb. 1. Vol. 10. No. 2. pp. 59–71. English summary p. 71. [Inst. of Trop. Path., Univ., Bologna.]

The author has conducted an experimental research regarding the question of the influence of super-infection of spirochaetes (*Sp. obermeieri. Sp. novyi,* and *Sp. duttoni*) in the case of trypanosomiasis (*T. brucei, T. evansi,* and *T. marocanum*) in rats, and has reached the conclusion that the spirochaetal infection has no influence on the course of trypanosomiasis.

W. Y.

KIKUTH (W.). Ueber die Behandlung der menschlichen Schlafkrankheit mit "Tryparsamid." [**Treatment of Human Trypanosomiasis with Tryparsamide.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1929. Jan. Vol. 33. No. 1. pp. 50–57. [43 refs.] [Inst. for Ship & Trop. Diseases, Hamburg.]

This article is a summary of the results hitherto obtained with tryparsamide in sleeping sickness: it contains nothing new.

W. Y.

BAKUNIN (Luigi). Contributo allo studio della terapia della tripanosomiasi.—*Arch. Ital. Sci. Med. Colon.* 1929. Jan. 1. Vol. 10. No. 1. pp. 31–35. English summary pp. 35–36. ["Garibaldi" Italian Hosp., Rosario, Argentine.]

SHIRCORE (J. O.). Infection with Trypanosomes of the Cerebro-Spinal Fluid by Lumbar Puncture. [Correspondence.]—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1928. Nov. 25. Vol. 22. No. 3. p. 301.

RABIES: A REVIEW OF RECENT ARTICLES. XI.*

i. *Virus.* The question of the occurrence of rabies in South Africa has been referred to in various reviews (this *Bulletin*, Vol. 24, p. 760, Vol. 25, p. 194). It will be remembered that though clinical and epidemiological evidence was not lacking, in no case had a definite pathological diagnosis been made. This lacuna has now been filled, and HERZENBERG[1] reports that Dr. BUCHANAN at the South African Medical Institute has demonstrated the presence of the virus in the brains of two boys, bitten by a red meerkat (*Cynictis penicillata*), who died from typical rabies. In the brain of the first, Negri bodies were not found, but inoculation killed two rabbits, in the brains of which the bodies were present. In the brain of the second atypical bodies were seen, and again the animal test was positive, with typical Negri bodies. Further sub-passages in both cases confirmed the diagnosis.

The more difficult problem of rabies in Equatorial Africa is further discussed by REMLINGER.[2] He recalls the fact that the character of paralytic rabies in the passage rabbit varies with the season, that whilst the incubation period remains unaltered, the duration of the sickness is prolonged in the summer months. As would be expected, natural rabies in tropical climates differs considerably from that observed in temperate zones. Symptoms may be moderated, and fury may be rare. These differences do not, however, imply a radical difference in the strains of the virus. REMLINGER and CURASSON have definitely proved the identity of the virus of "oulou fato" with that of rabies. REMLINGER, LEGER, and TEPPAZ have further shown that the street virus of Morocco behaves in exactly the same manner in Senegal and in Morocco as it does in Paris, and that the fixed virus of Paris behaves exactly in the same way in Dakar and in Tangier as it does in Paris. BENNET (*Vet. Jour.*, March, 1927) examined a virus from Kordofan, which could not for various reasons have been imported from Europe. It was transmissible to man by natural infection, and was, in fact, the ordinary virus of the street. In short no virus has so far been found whose virulence cannot be exalted by subpassage through rabbits, and which cannot infect man, and all the evidence is against its possible existence. REMLINGER rightly concludes that poly- or auto-vaccines are a superfluous complication of antirabic treatment, since there is no evidence of the existence in nature of plurality of strains of the virus.

Plurality of strain will no doubt continue to be brought forward as a reason for failure of treatment. For example, TEODORASCU[3] makes use of the hypothesis to explain four failures after treatment by Piscariu's and Högyes methods. He claims that treatment with fixed virus did not develop an immunity against his strains and, conversely, that vaccination with his strains was ineffective against ordinary

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* For the tenth of this series see Vol. 26, pp. 215–226.

1 HERZENBERG (L.). Two Cases of Hydrophobia.—*Jl. Med. Assoc. South Africa.* 1928. Dec. 22. Vol. 2. No. 24. pp. 659–661.

2 REMLINGER (P.). Quelques considérations sur la rage et le traitement antirabique dans les pays tropicaux.—*Bull. Soc. Path. Exot.* 1928. Nov. 14. Vol. 21. No. 9. pp. 790–797. [10 refs.]

3 TEODORASCU (C.). Etudes expérimentales sur la virulence particulière de deux souches de virus rabiques.—*C. R. Soc. Biol.* 1929. Apr. 8. Vol. 100. No. 11. pp. 929–930.

fixed virus when tested experimentally on rabbits. Before accepting his thesis one would require to be convinced as to the validity of the conclusions which he has drawn from his experiments. This would necessitate a fuller treatment than is given in his paper.

CALDERINI[4] has examined a strain of virus obtained originally from a cow, which after 35 passages (19 through guineapigs, 6 through rabbits, and again 10 through guineapigs) attained a virulence such that it could kill a guineapig on the fourth day. This hypervirulence was maintained after 26 further passages through guineapigs. The virus, so modified, preserved its virulence after being kept in 30 per cent. glycerine for 20 to 25 days. The author considers that this exaltation of virulence depended upon some inherent character which was present initially (i.e., in the cow), and that it was not a result of the subpassages through the guineapig. He has treated other strains of street virus in a similar manner, and in none of these, even after many subpassages, has he observed death of the guineapig in less than 5 days. These observations in his opinion confirm PUNTONI's views regarding plurality of strain.

MANOUELIAN and VIALA[5] starting from the well-known fact that Negri bodies are seldom seen in the spinal cord, whilst the virulence of this tissue proves that the virus is present, assume that the Negri body is an evidence of a defensive action of the nerve cells against the virus, and that the cells of the spinal cord are not so reactive as those of the hippocampus major. This reaction causes the germs to agglomerate into compact masses with the rough outline of Negri bodies, which with further development assume the rosette form of the typical body. Where there is little reaction the parasites may be abundant, but they remain in a diffuse condition. In fixed virus rabies there is no difference between the appearances seen in the cord and in the hippocampus. The virus is abundantly present in the cord of the dog, each section showing cells filled with small scattered parasites. In rabbits, both with street and fixed virus, considerable numbers may be observed. In suitable preparations the parasites may be so abundant that the cytoplasm and dendra of the cells stain red against a blue background. In the case of street virus agglutination may be observed.

GERLACH and SCHWEINBURG[6] submit an analysis of the presence of Negri bodies in the brains of 56 persons who died of rabies at the Vienna Institute during the years 1916–1928. Of these 35 were of untreated persons. In 30 of this number (86 per cent.) Negri bodies were found ; in the case of the remaining five, three of the brains were in a decomposed condition and in two the hippocampus could not be found. Twenty were from treated patients. These may be divided into two groups, (*a*) those who died within 14 days after completion of treatment, and (*b*) those who died at a later period. Nine brains related to the former class, and in 6 of these (66 per cent.) Negri bodies were present ; 12 to the latter, and in this group, 5 showed bodies (42 per cent.). To test the significance of this variation

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[4] CALDERINI (M.). Un caso di eccezionale esaltazione della virulenza del virus rabbico nella cavia.—*Giorn. di Batteriol. e Immunol.* Turin. 1928. June. Vol. 3. No. 6. pp. 429–434. [10 refs.]

[5] MANOUELIAN (Y.) & VIALA (J.). La moelle épinière, le bulbe, la protubérance et le parasite de la rage.—*C.R. Acad. Sci.* 1928. Dec. 10. Vol. 187. No. 24. pp. 1168–1170.

[6] GERLACH (F.) & SCHWEINBURG (F.). Ueber den Einfluss der Lyssaschutzimpfung auf die Entwicklung der Negrischen Körperchen.—*Cent. f. Bakt.* I. Abt. Orig. 1929. Vol. 110. No. 6/8. pp. 159–164.

experiments were carried out on rabbits. A group of 8 received a 13 days' course of treatment by Högyes method, the test dose of street virus being administered on the first day of treatment. Four out of the eight showed Negri bodies, usually small in size, whilst in untreated controls bodies of all sizes and forms were present. A further series received their test dose 8 and 14 days after the commencement of treatment. Five out of 9 showed no Negri bodies, but a few coccal forms, two showed numerous definite bodies, and one a few small bodies. The controls as before showed numerous bodies of all shapes and sizes. When the infecting dose was given at a still later date the difference was still more marked. The authors believe that this adds further support to the theory of the parasitic nature of the Negri bodies, that the coccal forms are early stages in the development of the parasite, which later develops into the mature body.

KRITSCHEWSKY[7] finds that a 10 per cent. glycerine emulsion of the Berlin fixed virus, kept on ice, retains its virulence for three months (as tested by intracerebral inoculation), and that the Berlin vaccine can well withstand such temperatures as it may be submitted to during transit to treatment centres in Germany. The emulsion, diluted to 1 in 25 for use as a vaccine, can safely be kept on ice until the evening.

In a previous communication (this *Bulletin*, Vol. 24, p. 765) HERRMANN[8] showed that loss of virulence is not always proportional to the period of desiccation, nor to the time of preservation in glycerine. He comes to a like conclusion from a further series of experiments on 22 rabbits which had been inoculated with cords which had been kept in glycerine on ice for long periods. After 5 months preservation one (incubation 10½ days) out of three succumbed; after 9 months two (6½ and 8½ days) out of three, after 11 months three (9, 53 and 54 days) out of three, after 12 months two rabbits showed symptoms of recurrent rabies, and both survived, after 12½ months three out of three survived. These experiments were carried out with pure sterilized glycerine.

The attention of those who are interested in neurotropic viruses in general is drawn to a full paper by NICOLAU, DIMANCESCO-NICOLAU and GALLOWAY.[9] In this the pathology of Borna's disease, herpes, vaccinia, polymyelitis, and rabies are fully described. The conclusions with regard to rabies, mainly have reference to its well-known neurotropic characters.

ii. *Symptoms.* A case of recurrent rabies in the dog is reported by CHINI,[10] which in the first subpassage gave rise to recurrent symptoms in the rabbit. The details are as follows. The dog exhibited ocular symptoms, with paresis of the legs, and change in disposition. It was kept under observation, and after 24 hours had so far recovered that

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7 KRITSCHEWSKY (N. L.). Die experimentelle Begründung der Berliner Methode der antirabischen Impfungen.—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1929. Vol. 60. No. 5/6. pp. 337–345. [10 refs.] [State Microbiol. Inst., Rostov on Don.]

8 HERRMANN (Otto). Ueber den Virulenzverlust des in Glyzerin konservierten fixen Virus.—*Cent. f. Bakt.* I. Abt. Orig. 1929. Jan. 2. Vol. 110. No. 1/3. pp. 45–47. [7 refs.] [State Inst. for Med. Research, Kasan.]

9 NICOLAU (S.), DIMANCESCO-NICOLAU (O.) & GALLOWAY (I. A.). Etude sur les septinévrites à ultravirus neurotropes.—*Ann. Inst. Pasteur.* 1929. Jan. Vol. 43. No. 1. pp. 1–88. With 41 figs. & 2 coloured plates. [Numerous refs.] [Pasteur Inst., Paris & National Inst. for Med. Research, London.]

10 CHINI (Virgilio). Osservazioni sulla cosidetta "rabbia ricorrente."—*Ann. d'Igiene.* 1928. Dec. Vol. 38. No. 12. pp. 1002–1011. [22 refs.] [General Med. Clinic, Univ., Padua.]

it was set free. After two days it became restless, with attacks of excitement. It was then killed. The brain was examined and Negri bodies were found. A rabbit was inoculated with an emulsion of the dog's brain. On the 15th day symptoms of paresis were observed, from which it soon recovered. On the 26th day symptoms reappeared, and it died on the 29th day after having been typically paralysed. Negri bodies were present in its brain. Further passages were carried out both with the dog's brain, and with the rabbit's brain. In each case virulence was lost at the 3rd passage. The virus was atypical in that incubations were prolonged, and that with successive subpassage virulence diminished. The author is of opinion that this is a peculiar strain of virus, and that PUNTONI's views as to the plurality of strains are further supported (ante, page 726).

WEBB and MULLER[11] describe in detail the clinical and pathological aspects of two cases of human rabies, and RICE[12] deals with two cases which contracted the disease in spite of treatment by Harris's method.

iii. *Diagnosis.* BOHLS[13] recommends the following staining method for the rapid demonstration of Negri bodies :—

A solution containing 0·9 gm. of Methylene blue, 1·5 gm. of Rosaniline violet, 125 cc. each of Glycerine and Methyl alcohol, is mixed, shaken and allowed to ripen. Impressions of the hippocampus are prepared, and to these a mixture containing 10 drops of the above staining fluid in 20 cc. of 1 in 50,000 KOH is applied for two minutes with heating. The preparation is dried and examined. Negri bodies take the acid stain. The dilution must be freshly prepared.

iv. *Pathology.* The infectivity of salivary glands before the appearance of symptoms has been further examined by JONESCO and TEODOSIO.[14] Ten dogs were inoculated subdurally with street virus. On the succeeding day a salivary gland was excised from each dog, emulsified, and inoculated subdurally into a rabbit. In 4 cases the gland proved virulent, that is to say, it had become virulent seven days before the appearance of rabies in the dog. In five cases it was avirulent but in each case the dog did not develop symptoms of rabies for more than seven days after the gland was excised.

Starting from the assumption that immunity against rabies is a tissue immunity, DE-GEORGES[15] has examined the effects of certain substances (alcohol, carbolic acid) which exercise an influence upon the haemato-encephalic barrier, by opening the path of penetration of the vaccine into the nervous tissue. A group of control rabbits received 1 to 2 cc. of fresh fixed virus in a dilution of 1 in 150 in normal salt solution,

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11 WEBB (U. R.) & MULLER (F. W.). Rabies. Report of Two Cases.—*U.S. Nav. Med. Bull.* 1929. Jan. Vol. 27. No. 1. pp. 98–111.

12 RICE (Thurman B.). Two Human Cases of Rabies.—*Jl. Amer. Med. Assoc.* 1928. Nov. 24. Vol. 91. No. 21. pp. 1631–1632.

13 BOHLS (S. W.). The Wilhite Stain for Negri Bodies.—*Jl. Lab. & Clin. Med.* 1929. Jan. Vol. 14. No. 4. p. 379.

14 JONESCO (Demètre) & TEODOSIO (V.). Passage du virus rabique dans les glandes sous-maxillaires chez le chien.—*C.R. Soc. Biol.* 1929. Apr. 8. Vol. 100. No. 11. pp. 897–898.

15 DE-GEORGES (L.). [Valeur de la barrière hémato-encéphalique dans l'immunisation contre la rage.]—*Rev. Microbiol., Epidémiol. et Parasit.* 1928. Vol. 7. No. 4. pp. 360–367. [25 refs.] [In Russian. French summary p. 457.]

intravenously. A second group received the same dose of vaccine, but had been injected previously with 2 cc. of a solution of 2 per cent. carbolic acid, or of 25 per cent. alcohol, also intravenously. These manipulations were repeated on two or three occasions with intervals of seven days. A month later all received an infecting dose of fixed virus. Of these 5 died during immunization, and 6 of shock. The subsequent history of the remaining 50 was as follows :—

	Number of rabbits.	Survived.
Controls	23	5
Treated with Alcohol	9	5
Treated with Carb. Acid	18	10

The author concludes that these substances by diminishing the normal resistance of the barrier, increased the immunizing effect by about 2½ times.

In view of the fact that Indian ink, injected *in vivo*, acts on the reticulo-endothelial system, in such a manner that the endothelial cells of the capillaries become specifically impregnated by the stain, MARIE[16] has examined the effect of such treatment upon infectivity of fixed virus introduced intramuscularly. The results of controlled experiments upon 42 mice were very contradictory, and the author concludes that sometimes the ink blocks the reticulo-endothelial system, and sometimes it fails to do so.

JONESCO and VALTER[17] have examined the effects of splenectomy in rabbits both upon the course of rabies infection, and upon the blood changes during rabies. The observation was carried out on 10 rabbits and had no effect upon the course of the disease. The leucocytosis was rather more intense in splenectomized than in control animals, but otherwise there was no essential difference.

FERMI and LUMBAU[18] compare the rabicidal with the "immunising" power of various anti-rabic sera. The rabicidal power is measured in terms of the proportion of serum which is necessary to neutralize 1 cc. of a 1 per cent. emulsion of Sassari fixed virus, tested by subcutaneous injection of 0·25 cc. of the mixture, after 24 hours contact, into white and grey mice. The immunizing power is determined as follows : Mice are infected by a subcutaneous inoculation of fixed virus under the skin, and after a certain period (24, 48, 72, 96 hours) a series of inoculations of the test serum (2 inoculations daily of 0·25 cc.) is commenced. A potent serum is found to be efficient even when the commencement of treatment is delayed for 96 hours after the animal has been infected. The strength of the serum is

16 MARIE (A. C.). Virus rabique et encre de Chine.—*C.R. Soc. Biol.* 1929. May 13. Vol. 101. No. 15. pp. 6–7.

17 JONESCO (Demètre) & VALTER (V.). Recherches expérimentales sur la splénectomie dans la rage.—*C.R. Soc. Biol.* 1929. Apr. 8. Vol. 100. No. 11. pp. 899–900.

18 FERMI (C.) & LUMBAU (Delio). Gibt es eine beständige Beziehung zwischen dem rabiziden Vermögen der antirabischen Seren und ihrem Immunisierungsvermögen? Zusammenfassung.—*Cent. f. Bakt.* I. Abt. Orig. 1929. Mar. 8. Vol. 111. No. 4/5. pp. 242–244.

indicated by the period of delay after which its administration is still able to save the animal. The results may be summarized as follows :—

Rabicidal power.	Period of delay.
1 : 10	96, 96.
2 : 10	48, 96, 96, 96, 84.
3 : 10	96, 0, 72, 84, 48, 84, 72, 84, 84.
4 : 10	72, 48, 72, 84, 72.
5 : 10	72, 72, 72, 72, 84, 84, 84.
6 : 10	72, 48.
7 : 10	24.
9 : 10	0.
Serum from normal horse	0.

Each of the figures in the second column of the above table refers to a particular serum. The number of experiments carried out to determine these values is not given.

It is stated that the dose of the Sassari fixed virus employed, and administered subcutaneously causes certain death. Two of the sera employed were withdrawn from human subjects one 15 days, and the other 4 days after completion of a 30 days course of treatment by Fermi's method. Both of these had rabicidal powers of 2 : 10, and both protected after a delay of 96 hours.

v. *Methods of Treatment.* As a result of the discussion at the International Conference, interest has been aroused regarding the effects of the various procedures which have from time to time been adopted in the production of vaccines. FERMI[19] examines the correlation between virulence of the strain of fixed virus employed and its immunizing action. He compares a virulent with an avirulent strain both as regards their protective properties when employed as a vaccine, and as regard the quantity of antibodies which they give rise to. A vaccine made with the virulent strain saved 8 out of 11, whilst one made with the avirulent saved 4 out of 12 animals of various type and variously treated. Also, the virulent strain gave rise to a serum which was able to save mice when administered 72 hours after infection, whilst the avirulent was only operative when given within 48 hours. The rabicidal power of serum produced by the virulent was in the proportion 4 : 10, whilst that from the avirulent was in the proportion 6 : 10. A repetition of this experiment gave a very similar result. Thus, he concludes that the Sassari virus, which is highly virulent, gives a more powerful vaccine, and calls forth a greater antibody response than does an avirulent strain. In a second paper FERMI[20] examines the effect of heating carbolized virus at 37° C. for 24 hours as is the characteristic of Semple's method. He refers to his experiments on this point which I have already quoted (this *Bulletin*, Vol. 25, p. 711) and adds the following further experiment. Twenty-four mice were

[19] FERMI (Claudio). Beeinflusst die Virulenz des fixen Virus die immunisierende Wirkung des antirabischen Impfstoffes und die Produktion des Antikörpers?—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1929. Vol. 59. No. 3/4. pp. 276–279.

[20] FERMI (Claudio). Beeinträchtigt die Erhitzung des karbolisierten Impfstoffes auf 37° C. während 24–72 Stunden die Wirksamkeit desselben?—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1929. Vol. 59. No. 3/4. pp. 280–284. [2 refs.]

infected with fixed virus, and three days later 12 of them received a three-day treatment of 3 daily doses of 0·25 cc. of carbolized vaccine kept at 37° C. The remaining 12 were treated similarly with carbolized virus which had been kept at 20° C. Of the former, 6 died of rabies, of the latter all survived. He concludes that Semple's vaccine is less active than his own, and quotes statistics of treatment showing that the mortalities at Institutes where his unheated vaccine is used are zero (Messina, Chicago, and Santa Clara) and 0·16 per cent. (Rome), whereas with Semple's vaccine they vary from 0·32 to 1·23 per cent. Omsk, Kasauli, Coonoor, Bombay, Calcutta, Shillong, Rangoon, Shanghai, and Jerusalem). It will be observed, however, that all the latter group of Institutes are in Asia (*see* this *Bulletin*, Vol. 25, p. 712). We must correct a statement of FERMI's that at Kasauli a return has been made to FERMI's original method. This is not the case. In a further paper FERMI[21] contrasts experimental results upon mice and rats with his carbolized vaccine and with glycerine vaccine. His results may be summarized as follows :—

	Carbolized vaccine.	Glycerine vaccine.
Survived	62	44
Died of Rabies	28	46

The probability that a disagreement equal to or greater than the observed might arise from random causes is of the order of 1 in 100.

FERMI[22], [23] regards phenol as the best antiseptic for use in preparing vaccines. The phenol has no immunizing properties *per se*; it does not, as employed in his method, reduce immunizing properties, and in the doses used it is non-toxic.

TORRES,[24] following SCHNÜRER and DAVID, and DE GEORGES (this *Bulletin*, Vol. 24, p. 769 and 229 respectively), has found that sera of guineapigs treated on 8 consecutive days by percutaneous application, with friction, of a phenol glycerinated vaccine, and withdrawn 23 days after the last dose, if used in sufficiently high concentrations, are capable of inactivating fixed virus. Normal guineapig serum had no inhibiting action.

21 FERMI (Claudio). Karbol- oder Glyzerinimpfstoffe gegen Wut.—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1929. Vol. 61. No. 1/2. pp. 91–98. [2 refs.]

22 FERMI (Claudio). Il fenolo è ancor sempre il migliore antisettico nella preparazione del vaccino antirabbico, di cui aumenta pure l'efficacia.—*Policlinico.* Sez. Prat. 1929. Feb. 4. Vol. 36. No. 5. pp. 153–155. [5 refs.]

——. La dose giornaliera di fenolo iniettata col vaccino antirabbico fenicato non è tossica.—*Ibid.* pp. 155–156. [6 refs.]

23 FERMI (Claudio). Welches ist gegenwärtig das beste Antiseptikum bei der Herstellung des Impfstoffes gegen die Wutkrankheit?—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1929. Vol. 60. No. 5/6. pp. 377–380. [5 refs.]

24 TORRES (Sylvio). Contribuiçã ao estudo da immunidade local na raiva. O sôro das cobayas vaccinadas por via dermica contêm substancias rabicidas?—*Rev. Zootechnia e Vet.* 1928. Vol. 14. No. 3. pp. 197–201.

25 PONOMAREW (A. W.) & SOLOVIEW (N. N.). Une nouvelle méthode de préparation de vaccin antirabique et un essai d'utilisation de ce vaccin pour la préparation d'un sérum antirabique d'une activité élevée.—*Arch. Sci. Biol.* 1928. Vol. 28. No. 3. pp. 325–334. [31 refs.] [In Russian. French summary pp. 376–377.]

An attempt has been made by PONOMAREW and SOLOVIEW[25], [26] to remove as much nervous tissue as possible from vaccinal material with the object of reducing its toxic action. The procedure is as follows :—

A 1 per cent. emulsion of brain substance is kept on ice for some hours, the supernatant fluid is decanted, and to it is added one-quarter of its volume of liquid paraffin. The mixture after having been shaken for one or more hours, is centrifuged for 30 minutes. A feebly opalescent fluid is obtained, above and below which are layers of nervous debris. This transparent fluid is pipetted off. The liquid paraffin is then replaced by ether and separated off by centrifugation.

With this vaccine horses have been hyper-immunized. No neurotoxins are formed as heterologous brain substance has been as far as possible removed. The serum of horses so treated is highly active. It neutralized 1 per cent. fixed virus in dilutions of 1-1,000 to 1-3,000. Ten cubic centimetres injected intravenously prevented rabies in 50 per cent. of rabbits which had received 1 to 2 lethal doses of fixed virus suboccipitally, and 20 cc. saved 70 per cent.

The method of treatment employed by STUART and KRIKORIAN[27] at Jerusalem is that of SEMPLE, modified in that the primary emulsion which is heated with 1 per cent. phenol at 37° C. for 24 hours, is of a concentration of 8 per cent. brain substance, whereas in Semple's procedure a 2 per cent. emulsion is employed. With a dosage of 0·28 gm. of brain substance (1923–1924) 9 out of 748 treated persons died, whereas with a dosage of 0·7 gm. (1924–1928) 5 out of 2,412 developed rabies. The following experiments regarding the effects of carbolization (as above described) are instructive :—

No. of Rats.	Daily dose of 2 per cent. Vaccine.	Died.	Survived.	Percentage Immunity.
10	1 cc. carbolized	5	5	50
10	1·5 cc. carbolized	2	8	80
10	2 cc. carbolized	4	6	60
8	2·5 cc. carbolized	5	3	37
9	1 cc. in saline	3	6	66
10	1·5 cc. in saline	2	8	80
10	2 cc. in saline	4	6	60
8	2·5 cc. in saline	3	5	62

The effect of carbolization (as above described) is inappreciable; the highest degree of immunity in each case was obtained with doses of 1·5 cc., i.e., 750 mgm. per kilo of body-weight.

They then compared the two methods of treatment in respect of the rabicidal activity of the sera of animals so treated, and found that whilst with uncarbolized vaccine, a demonstrable effect could be detected 12 days after completion of treatment, and a maximum (1 unit neutralized 16 units of 1 per cent. fixed virus) was attained about the 38th day, with carbolized vaccine the maximum was lower (1 unit

[26] PONOMAREFF (A. W.) & SOLOVIEFF (N. N.). Nouveau procédé de la préparation du vaccin antirabique et essai d'application de ce vaccin pour l'obtention d'un sérum antirabique de haute activité.—*Ann. Inst. Pasteur* 1928. Dec. Vol. 42. No. 12. pp. 1661–1671. [18 refs.] [Inst. of Experim. Med., Leningrad.]

[27] STUART (G.) & KRIKORIAN (K. S.). Studies in Anti-Rabies Immunisation.—*Jl. of Hyg.* 1929. Apr. Vol. 29. No. 1. pp. 1–34. With 1 chart in text. [61 refs.] [Dept. of Health, Palestine.]

neutralized 8 units). Using the sera obtained by both methods of treatment and alcoholic brain extract as antigen, they were unable to demonstrate any complement binding activity. From experiments on 70 rabbits in batches of 10, in which carbolized vaccines were heated at 37° C. for periods varying from 26 to 168 hours, it appeared that the vaccine became avirulent after 144 hours exposure to heat. A further interesting series of observations was made to determine how far distribution of dosage influenced the efficacy of treatment. Four rabbits received a treatment of 2 cc. daily for 14 days (in all 200 mgm. per kilo of body-weight), four received doses of 4 cc. for 14 days (400 mgms. per kilo), four received doses of 6 cc. for 10 days (430 mgm. per kilo), four received doses of 15 cc. for 3 days (320 mgm. per kilo), and four received a single injection of 30 cc. (214 mgm. per kilo). Unfortunately, the table cited in the text has dropped out in publication, but the authors state that better results followed a 14 days' treatment with a small daily dose, than larger doses given over a shorter period.

Reference may here be made to an observation by FERMI[28] of a similar nature. He found that mice which received 15 cc. of vaccine during a period of 30 days, were more refractory than others which received 30 cc. during a period of 6 days. From this and other experiments he concludes that short intensive treatments with live vaccines are not only less effective, but may also be dangerous.

In another experiment he treated 10 dogs with 6, 5, 4, 3, 1 and 0 day dried cords at half-hourly intervals, and subsequently tested them with street virus. All died of rabies, seven of them from the fixed virus contained in the vaccine.

In the final section of their paper STUART and KRIKORIAN[27] consider the applicability of living fresh virus to treatment. Fresh virus is admittedly unsafe, but at the same time it has immunizing properties. FERRAN (1888) was of opinion that large doses were not so dangerous as small. The authors in the first place treated a number of rabbits with varying numbers of daily doses, each of which was 5 cc. of a 2 per cent. suspension of fixed virus in physiological salt solution. The results of three consecutive experiments were as follows :—

	No. of Rabbits.	No. of Daily doses.	Died.	Survived.	Percentage deaths.
Expt. I ...	5	5	3	2	60
	5	10	0	5	0
Expt. II ...	5	5	3	2	60
	5	10	0	5	0
Expt. III ...	5	7	2	3	40
	5	14	0	5	0

This suggested a further determination of the smallest number of daily doses which caused infection, and the smallest number which established complete immunity. For this purpose the following experiment was carried out, in which each dose was again 5 cc. of a 2 per cent. fixed virus in saline.

28 FERMI (Claudio). Ueber die Wirkung der antirabischen, intensiven und verlängerten Impfungen.—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1929. Vol. 59. No. 3/4. pp. 285–287. [5 refs.]

	No. of Rabbits.	No. of Daily doses.	Died.	Survived.	Percentage deaths.
Series 1 ...	5	1	0	5	0
2 ...	5	2	4	1	80
3 ...	5	3	2	3	40
4 ...	5	8	0	5	0
5 ...	5	9	0	5	0
6 ...	5	10	0	5	0

The results are strikingly uniform, and the authors conclude that the effect on rabbits of subcutaneous injections of living virus it dependent on the quantity administered, and the duration of the period of its administration. Few inoculations are more likely to cause death than several. As deaths from fixed virus administered subcutaneously occurred in 11 or 12 days from the commencement of treatment, the immunity which was acquired must have been produced within that period.

The last paper of this group is by FERMI,[29] and deals with destruction of the virus at the seat of inoculation. He has found that injection of 1 in 10,000 sublimate, 1 in 1,000 silver nitrate, 1 in 5,000 Tachyol, 1 in 1,000 Ichtargan, 1 in 200 protargol, 2 in 100 phenol, and 1 in 200 methylene blue solutions can save rats with certainty if performed immediately, but if delayed for 15 minutes the treatment is ineffective. He also found that absorption of the virus through the healthy nasal and rectal mucus membrane is so rapid that after 15 minutes none can be saved by thorough douching with thymol sublimate. Local treatment after 15 minutes with 2 per cent. phenol, or with 1 per cent. sublimate solutions are alike ineffective. Dipping in 20 to 50 per cent. nitric acid (" Nytriosäure ") was more effective than either cauterization or other antiseptics. Amputation of the tail seemed to be effective when performed even 5 hours after the tip was infected. Bier's hyperaemia saved all animals (rats, rabbits and dogs) when induced 4 hours after the infection. The hyperaemia was more effective than cauterization. With the former treatment 3/4 of the rabbits tested were saved, with the latter half were saved.

vi. *Statistics.* The statistics of antirabic vaccination in Germany for the year 1928 are reviewed by HESSE[30] according to the scheme which, on the recommendation of the International Conference, has been adopted by the League of Nations. In all, 376 were treated, all of whom were Europeans. At one institute (Breslau) Semple's vaccine is used. The other institutes all employ the method of Högyes-Phillips. The figures may be summarized as follows :—

	Vaccine.		
	Semple's.	Högyes-Phillips.	Totals.
Died	0	2	2
Survived	136	238	374
Totals	136	240	376

[29] FERMI (Claudio). Ueber die Lokalneutralisierung des " Virus rabicus."—*Zent. f. Bakt.* I. Abt. Orig. 1929. May 10. Vol. 112. No. 1/2. p. 73.

[30] HESSE (Erich). Die Tätigkeit der deutschen Wutschutzstationen im Jahre 1928.—*Reichs-Gesundheitsblatt.* 1929. May 8. Vol. 4. No. 19. pp. 380–383.

These figures afford no significant evidence in favour of either method of treatment. On the assumption that the two groups were samples of the same population and that the two methods of treatment were equally effective, figures such as the above would be quite likely to occur as the result of chance. As figures accumulate during ensuing years, it may be possible to assess the relative efficacies of the two methods. At present all one can say is that there is no evidence of inequality.

TSEN[31] reports that at the Peking Institute treatment by dried cords was employed from 1919 to 1923, whilst from 1923 to 1927 both dried cords and Semple's vaccine were used, and, since the latter date, Semple's treatment has been employed for all cases. He states that the mortality rates have not altered throughout the period.

OUCHAKOW[32] states that at the "Institut de Médecine expérimentale," three deaths occurred amongst 1,192 persons (0·25 per cent.) treated with Fermi's vaccine. Two cases of paraplegia were observed, one of which was fatal. The brain of the latter person did not infect rabbits.

GLOSTER[33] from Coonoor reports four deaths amongst 394 persons treated at the institute, and 45 out of 4,788 treated at out centres, with Semple's vaccine.

From Kasauli MALONE[34] reports 105 deaths amongst 6,041 Indians (a mortality of 1·74 per cent.), and 0 deaths amongst 281 Europeans, treated at the Institute. Reports regarding the state of health after 6 months, of 82 per cent. of the patients have been received. The treatment employed for cases of lesser severity was that of Semple, for those of greater severity ether vaccines were employed. Details of the methods, the populations at risk, and the relative results of the two types of treatment are being prepared in accordance with the resolution of the International Conference, and will be published later. A case is reported in which the patient died from hydrophobia 11 days after having been bitten on the bare skin of the foot, and 6 days after the commencement of treatment. The method of treatment employed is not stated.

vii. *Paralytic Accidents.* A case of paralytic accident in an experimentally infected dog is described by MARKOWSKI and LEGEZYNSKI[35] in which symptoms in the forelegs, and in the neck appeared 12 days after infection, and 10 days after commencement of treatment. Death supervened after six days. Negri bodies were not found in the brain ; nine rabbits inoculated with nerve substance all died of a pasteurella infection in 16 to 20 hours.

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31 TSEN (Edgar T. H.) & CHI (C. C.). The Preparation and Use of Phenolized Rabies Vaccine.—*Nat. Med. Jl. China.* 1928. Dec. Vol. 14. No. 6. pp. 402–409. [6 refs.] [National Epidemic Prevention Bureau, Peking.]

32 OUCHAKOW (W. G.). Service antirabique de l'Institut de Médecine expérimentale. (Rapport annuel pour 1927).—*Arch. Sci. Biol.* 1928. Vol. 28. No. 3. pp. 313–324. [In Russian. French summary pp. 375–376.]

33 COONOOR, SOUTHERN INDIA. Pasteur Institute. The Annual Report of the Director [GLOSTER (T. H.).] together with the Twenty-First Annual Report of the Central Committee of the Association for the Year ending 29th February 1928.—33 pp. 1928. Madras.

34 KASAULI. Pasteur Institute of India. The Twenty-Seventh Annual Report of the Central Committee of the Association and the Audited Accounts up to June 30th 1928. Also the Report of the Director of the Institute for the Year ending 31st December 1927. Part II. [MALONE (R. H.), Offg. Director.]—61 pp.

35 MARKOWSKI (Sigismond) & LEGEZYNSKI (Stanislaw). Sur un cas de paralysie postvaccinale chez un chien.—*C.R. Soc. Biol.* 1929. Feb. 1. Vol. 100. No. 4. pp. 291–292. [1 ref.]

viii. *Rabies in Animals.* BOUGHTON[36] describes the methods of control which have been adopted at Port-au-Prince, in the island of Haiti. Since 1926 stray dogs have been impounded and, if unclaimed, destroyed. Private dogs may not be taken on to the streets except when muzzled or on the leash. Latterly, all private dogs have been licensed, and vaccinated. Rabies in dogs is a notifiable disease, and suspects are isolated. During the year 1926–27, 367 dogs were vaccinated by Umeno and Doi's method, 36 brains were examined for Negri bodies, 19 of which were positive, and 2,962 unclaimed dogs were destroyed. Two of the 367 vaccinated dogs contracted rabies.

During the year 1927–1928, 347 dogs were vaccinated, 19 brains were examined of which 12 were positive, and 1,670 unclaimed dogs were destroyed.

According to STANHOPE[37] rabies is less prevalent in Malaya than in India and Siam. This he ascribes to the absence of the jackal, and to the lack of religious difficulties regarding the destruction of dogs. The Zerigala, or wild dog of this country, is rarely seen. An outbreak of rabies is at present occurring in Negri Sembilan, and 37 cases of rabies in animals have been reported since 1926. Dogs are registered, and taxed. During 1926, 9,000 unregistered dogs were destroyed. 520 dogs have been treated by the Japanese method with encouraging results. Local quarantine measures between the different states are discussed.

REMLINGER and BAILLY[38, 39] contribute an interesting study of rabies in the cock. Eleven cases of rabies in experimentally infected cocks are described in detail, and the pathological changes which were observed are discussed. In one which was bitten on the crest by a dog, symptoms of inco-ordination developed after 93 days, a week or so later amelioration was noted, and after about 120 days the animal recovered. It was noted that salivation is a frequent symptom in the cock. Five experiments were made to see whether transmission from bird to bird was possible by the peck of the beak, and in one of these a successful transmission followed. The research was undertaken on hearing of two cases where human beings had been pecked by enraged cocks. It would seem that the vaccinator must be prepared for the occurrence of such cases.

Four cases of rabies in horses are described by FINIK and MGLEJ[40] One of these was characterized by hypersensitivity of the skin, and twitching at the site of the bite.

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36 BOUGHTON (I. B.). Rabies Control in Port-au-Prince, Haiti.—*Jl. Amer. Vet. Med. Assoc.* 1929. May. Vol. 74. New Ser. Vol. 27. No. 6. pp. 921–924.

37 STANHOPE (R. A. B.). Rabies in Malaya.—*Vet. Rec.* 1928. Nov. 24. Vol. 8. No. 47. pp. 999–1004. [9 refs.]

38 REMLINGER (P.) & BAILLY (J.). La rage du coq.—*Bull. Acad. Méd.* 1929. Jan. 22. Year 93. 3rd Ser. Vol. 101. No. 3. pp. 103–109. [2 refs.].

39 REMLINGER (P.) & BAILLY (J.). La rage du coq.—*Ann. Inst. Pasteur.* 1929. Feb. Vol. 43. No. 2. pp. 153–167. [1 ref.]

40 FINIK (Zdzislaw) & MGLEJ (Stanislaw). Zur Kasuistik der Tollwut bei Pferden.—*Berlin Tierärzt. Woch.* 1929. Jan. 11. Vol. 45. No. 2. pp. 20–22. [5 refs.] [Vet. High School, Lemberg.]

41 BIGOT (A.), EYRAUD (R.) & VELU (H.). Nouveaux essais de vaccination antirabique préventive du chien.—*Bull. Acad. Vét. de France.* 1929. Jan. Vol. 2. pp. 61–68. [4 refs.]

42 VELU (H.), BIGOT (A.) & EYRAUD (R.). Au sujet de la vaccination préventive des chiens contre la rage.—*C.R. Soc. Biol.* 1928. Dec. 14. Vol. 99. No. 36. pp. 1774–1775. [2 refs.]

BIGOT, EYRAUD and VELU[41, 42] claim that if vaccination by the Japanese method is followed three weeks later by a small injection of fresh fixed virus, a solid immunity is conferred which lasts for 5 or more months. A repetition of this living dose converts this immunity into a hyper-immunity. These conclusions are based on an experiment on 12 dogs, inoculated at the first instance with 5 cc. of carbolized vaccine subcutaneously on the abdomen. The subsequent living dose was 5 cc. of fresh fixed virus. A series of test inoculations was made, each thoroughly controlled, with the result above stated.

KARMANN[43] compares the immunizing potencies of Fermi's, Umeno and Doi's and Miessner's Lyssin vaccines. From controlled experiments with the three methods he concludes that single doses give a definite immunity. With Fermi's vaccine three out of four survived, with the Japanese method six out of six, with Lyssin six out of six, whilst of untreated controls one out of four survived, the test dose being given 67 days after treatment. In a second experiment the test dose was given after 179 days, and in this case with Fermi's vaccine three out of four survived, with the Japanese vaccine nine out of nine, with Lyssin nine out of nine, whilst of the untreated controls four out of six survived. In a third experiment in which Lyssin was alone employed, 23 out of 29 treated dogs survived a test dose given 86 days later, whilst of the untreated two out of thirteen survived.

MARGINESU[44] has treated 47 dogs by the Japanese method, 20 with a single dose, and 27 with three injections of 3 to 5 cc. according to weight. The author observed no ill-effects from the treatment, and none of the dogs acquired rabies during the succeeding six months. He was unable to demonstrate any rabicidal action in the sera of any of these animals.

MARKOWSKI and LEGEZYNSKI[45] examined the curative value of Fermi's vaccine on artificially infected dogs. The infecting dose was 5 to 6 cc. of 1 per cent. street virus. Of 8 dogs whose treatment commenced 45 hours after the infective dose was given, 4 resisted, whilst of 4 untreated dogs and 4 untreated rabbits all died of rabies. Of 8 dogs whose treatment was commenced 21 hours after infection, 5 resisted, whilst of 4 untreated dogs one survived, and of 4 untreated rabbits all died.

REMLINGER and BAILLY[46, 47] describe in detail their experiences of vaccination of dogs in Morocco by Remlinger's ether vaccines (this

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43 KARMANN (P.). Zur Frage der Schutzimpfung der Hunde gegen die Tollwut.—*Deut. Tierärzt. Woch.* 1928. Dec. 8. Vol. 36. No. 49. pp. 817–823. With 1 text fig. [39 refs.]

44 MARGINESU (P.). Ricerche sul potere lissicida ed immunizzante del siero di cani vaccinati col metodo giapponese "Umeno e Doi."—*Giorn. di Clin. Med.* 1929. Feb. 10. Vol. 10. No. 2. pp. 67–82. [Hyg. Inst., Univ., Parma.]

45 MARKOWSKI (Sigismond) & LEGEZYNSKI (Stanislaw). Recherches expérimentales sur la vaccination antirabique curative des chiens.—*C.R. Soc. Biol.* 1929. Feb. 1. Vol. 100. No. 4. pp. 289–290. [1 ref.]

46 REMLINGER (P.) & BAILLY (J.). La vaccination antirabique du chien au Maroc.—*Bull. Acad. Méd.* 1929. Mar. 12. Year 93. 3rd Ser. Vol. 101. No. 10. pp. 366–374. [8 refs.]

47 REMLINGER (P.) & BAILLY (J.). La vaccination antirabique du chien au Maroc.—*Rev. Gén. de Méd. Vét.* 1929. Apr. 15. Vol. 38. No. 448. pp. 193–200. [8 refs.]

Bulletin, Vol. 22, p. 704). Of 234 dogs treated prophylactically, and 30 which had been bitten in natural circumstances by rabid dogs, 2 of the former group and none of the latter developed rabies. The ether vaccine in their opinion owes its power not only to the living virus contained in it but to the quantity which can be employed (120 cc.). It will be remembered that the treatment consists of three doses, the first of fixed virus which has been operated on by ether for 25 hours the second for 20 hours, and the third for 15 hours, the dose in each case being the equivalent of one brain. VALLÉE[48] in a report on this communication strongly recommends the method.

USTUPNY[49] using doses of 0·3 to 1 gm. of fixed virus at first in normal salt solution, and later in glycerine has treated 225 dogs during the period 1920–1927. Only one of these developed rabies. He believes that the vaccine so prepared is more active than carbolized vaccines or "lyssin." From a limited experiment he concludes that doses of more than 1 gm. are dangerous.

ix. *Miscellaneous.* PONOMAREW[50] recommends sub-occipital puncture in the experimental transmission of rabies. The animal is anaesthetized, and the skin suitably prepared. The tip of the index finger of the right hand then is placed on the space between the occipital bone and the atlas, and guides the point of the syringe into the interval. A small quantity of cerebro-spinal fluid is withdrawn, and the barrel of the syringe is detached. Thereafter a dose of 1 cc. may be easily injected into the rabbit, and a dose up to 10 cc. into the dog. He recommends the method especially in experiments where accuracy of dosage is of importance. It has been successfully used on 300 rabbits.

SCHERN[51] describes a simple instrument for trephining rabbits. It consists of a flat strip of metal, through the end of which, and perpendicular to the flat surface, a part like a large drawing pin is screwed. The strip is continued into a handle which is grasped in the fingers, the thumb pressing on the head of the drawing pin. The skull is perforated by pressing the thumb; the depth of the perforation depends upon the adjustment of the screwed pin.

PHISALIX and PASTEUR[52] bring forward further experiments which show that exposure to ultra-violet rays kills the rabies virus.

MOOSER[53] finds that of 34 rats immune to recurrent fever, the *Spirochaeta duttoni* can be demonstrated in the blood three months after

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48 VALLÉE et al. Sur la vaccination antirabique, selon la méthode de Remlinger. —*Bull. Acad. Méd.* 1929. May 14. 93rd Year. 3rd Ser. Vol. 101. No. 18. pp. 604–606.

49 USTUPNY (D. I.). Ueber Immunisierung der Hunde und anderer Tiere gegen die Tollwut.—*Cent. f. Bakt* I. Abt. Orig. 1929. Jan. 11. Vol. 110. No. 4/5. pp. 175–180. [9 refs.] [Microbiol. Inst., Rostov a.D.]

50 PONOMAREW (A. W.). [La piqure sous-occipitale comme méthode d'infection rabique par l'espace sous-arachnoïdien.]—*Arch. Sci. Biol.* 1929. Vol. 29. No. 1. pp. 75–81. With 2 text figs. [10 refs.] [In Russian. French summary pp. 82–84.]

51 SCHERN (K.). Ein einfaches Instrument als Trepanersatz zur subduralen Infektion von Kaninchen, speziell mit Tollwutvirus.—*Deut. Tierärzt. Woch.* 1929. Apr. 13. Vol. 37. No. 15. pp. 235–236. With 2 text figs.

52 PHISALIX & PASTEUR (F.). Action des rayons ultra-violets sur le virus rabique et ses antigènes rabique et venimeux.—*C.R. Acad. Sci.* 1929. Jan. 14. Vol. 188. No. 3. pp. 276–278. [1 ref.]

53 MOOSER (Hermann). Ueber den Einfluss der Wutinfektion auf die Gehirnspirochäten-Rekurrens immuner Ratten.—*Arch. f. Schiffs- u. Trop.-Hyg.* 1929. Feb. Vol. 33. No. 2. pp. 83–92. [11 refs.]

infection, in all cases. Whilst of 27 rats similarly immune but also artificially infected with rabies the spirochaete was observed in only 56 per cent. This disappearance of the spirochaete is explained as due to increased permeability of the vascular endothelium in brains which have been changed by encephalitis.

PHISALIX[54] believes that all sera which are naturally antirabic, are also antivenemous. The converse is, however, not always the case. Natural antivenemous sera are not all antirabic.

LAUGHINGHOUSE[55] discusses the possibility of eradicating rabies from the Southern States of America. He favours the adoption of muzzling, and destruction of ownerless dogs, rather than prophylactic vaccination.

A. G. McKendrick.

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54 PHISALIX. Sur quelques propriétés comparées des sérums antirabiques d'animaux vaccinés et celles des sérums antirabiques naturels.—*C.R. Acad. Sci.* 1929. Apr. 22. Vol. 188. No. 17. pp. 1126–1128.

55 LAUGHINGHOUSE (Charles O'H.). The Prevention of Rabies by Legislative Enactment.—*Southern Med. Jl.* 1929. May. Vol. 22. No. 5. pp. 503–504.

KALA AZAR.

NICOLLE (Charles) & ANDERSON (Charles). Chronique du kala azar en Tunisie. [**Reports of Kala Azar in Tunis.**]—*Arch. Inst. Pasteur de Tunis.* 1929. Mar. Vol. 18. No. 1. pp. 63–70. [1 ref.]

Up to the year 1925 there had been observed in Tunis, 67 cases of kala azar (this *Bulletin* Vol. 22. p. 687). In addition, six further cases have been recorded while twelve are now noted for the first time. In all, 85 cases, all diagnosed by spleen puncture, have been seen. Of the 85 cases, the parents of 58 were Italian, those of 11 French, those of 4 French and Italian, and those of 4 others, Maltese. The parents of one were French and Maltese. Four of the cases were in native Mohammedans and 3 in native Jews. The frequence amongst the Italians is very remarkable, but no explanation of this is given. As regards age incidence the following figures are given: 5 to 6 months, 2; 6 months to 1 year, 10; 1 to 2 years, 29; 2 to 3 years, 15; 3 to 4 years, 8; 4 to 5 years, 5; 5 to 6 years, 7; 6 to 7 years, 4; 8 to 10 years, 2; 21, 25, and 38 years, 3.

Referring to cultures, the authors state that they have several strains which they will be glad to supply to investigators who require them. They are: (1) Human kala azar, five strains isolated in September 1910, February 1912, August 1918, December 1926 and April 1927. Up to December 1928 these have been subcultured 499, 449, 267, 53 and 43 times respectively. (2) Canine kala azar, two strains isolated in December 1911 and February 1913 and subcultured 449 and 438 times respectively. (3) Oriental sore, four strains isolated in 1909, November 1919, December 1919 and April 1926, and subcultured 488, 236, 234 and 70 times. The second strain is actually the same as the first which was inoculated into man and reisolated in November 1919. (4) Leptomonas of the gecko. Two strains isolated by CHATTON at Dehibat in April and May 1917, and subcultured 302 times, and two strains isolated at Tamerza in October, 1919 and subcultured 238 times.

C. M. Wenyon.

JEMMA (R.). Sulla endemia di leishmaniosi infantile in Italia. [**Endemicity of Infantile Leishmaniasis in Italy.**]—*Pediatria.* 1929. Feb. 1. Vol. 37. No. 3. pp. 113–118. [Pediat. Clinic, Univ., Naples.]

The paper is one which was presented at the Congress of Tropical Medicine and Hygiene held in Cairo in 1928, and deals with the endemicity of kala azar in Italy. It is most prevalent in the Provinces of Naples and Catania. Up to 1914, 110 cases were seen at the Clinica Pediatrica at Palermo, while the author was director, and 119 cases since then by his successor DI CRISTINA. At Catania 1,400 cases have been seen by LONGO, 180 cases by CANNATA at Messina, 20 by MAGGIORE and MALLARDI at Bari, and 30 others by various other observers. Of the total of about 2,400 cases, about two-thirds have been seen during the last ten years. Up to 1925 in the Province of Naples, the cases seen annually increased up to a maximum of 73. During the last three years there has been a decline to an average of 50. The improvements in hygiene and the standard of living under the Fascist régime may have lessened the morbidity rate, for the number of patients seen at the clinics has certainly decreased. The outstanding feature of the disease is the great change which has taken place since the introduction of

treatment with tartar emetic. A recovery rate of 10 per cent. in the pre-tartar emetic days has been converted into one of 90 per cent. Statistics of 551 observations give a general cure rate of 78 per cent. In 1928 this had increased to 90 per cent. In the author's experience, the organic antimony compounds, such as urea stibamine and stibosan, though well tolerated and administrable by intramuscular injection, are no more curative than tartar emetic.

C. M. W.

YOUNG (Charles W.) & HERTIG (Marshall). **The Kala Azar Transmission Problem: Field and Laboratory Studies in China. I. Epidemiology.**—*Amer. Jl. Hyg.* 1929. Jan. Vol. 9. No. 1. pp. 227–246. With 2 text figs. [29 refs.] [Peking Union Med. College, Peking.]

This paper is the first of a series in which it is proposed to describe the work done in China, during the four years 1924 to 1927, on the kala azar transmission problem. It deals especially with general considerations regarding the epidemiology of the disease.

The endemic area in North China is substantially that noted by COCHRAN in 1912. It occupies roughly the whole of the coastal plain north of the Huai River, from the hills of Shansi to the coast and bounded on the north by the Great Wall. The most heavily infected area is roughly a belt in the region of the old course of the Yellow River from the Province of Honan to the sea, with the heaviest centre near the Grand Canal. The disease is not known to occur in Korea or Japan. The early history of the disease in China is unknown. There has been no great epidemic like that in Assam. The disease tends to occur in cycles of fifteen to twenty years, but the incidence in each area or village may have no relationship to that in neighbouring ones. The cycle is characterized by a mild epidemic lasting four or five years, followed by a decline to few or no cases for ten or fifteen years. The incidence is characteristically sporadic, successive cases in a village showing no obvious relationship to previous ones. Furthermore, there is no evidence of any seasonal variation in the incidence of cases as first pointed out by PATTON and HINDLE. This may be of significance when taken into consideration with the definite sand fly season of the end of May to the end of September. Mention is made of a case noted by HINDLE in which an infant four months old was admitted to hospital in Tientsin with the disease, in March. In such a case, however, the possibility of infection from the mother has to be taken into account.

The incidence of kala azar is definitely rural and no large city is known to have much of the disease. The infected areas, as in India, are chiefly flat plains of deep alluvial soil, while most of the rural regions in the endemic area are subject to floods during the rainy season of June and July. At other times of the year where there is little rainfall, the land may be dry and approaching semi-aridity. In other parts, with a rainfall of about 25 inches, the country is less dry. Wheat is raised everywhere and forms the chief article of diet. Neither rice nor bamboo are grown and it is noteworthy that these are replaced abruptly by wheat fields at the Huai River, the southern limit of the disease. Examining the various conditions the authors have been unable to determine any single factor characteristically associated with kala azar in China, nor have they been able to distinguish any feature characteristic of infected villages or houses.

On the subject of transmission the various theories which have been advanced are reviewed. Reference is made to the discovery of the susceptibility to inoculation of the hamster. Attempts to discover a reservoir of infection in the hamster or other animal failed. Attention was paid especially to the sand fly, but the problem is still unsolved. The fact elucidated that leishmania injected into the coelom of sand flies will flagellate and persist for nine days, while they will behave similarly and persist for at least forty days in the bed bug, raises the question as to whether such a devleopment is any indication of the specificity of the organism for the particular arthropods. These and other features of the work will be discussed in subsequent communications.

C. M. W.

Hu (C. H.) & Lee (C. U.). **New Technique for feeding Sandflies (Phlebotomus) for Experimental Transmission of Kala-Azar.**—*Proc. Soc. Experim. Biol. & Med.* 1929. Jan. Vol. 26. No. 4. pp. 277–280. With 2 text figs. [2 refs.] [Peking Union Med. College, Peking, China.]

The authors describe a method for feeding sandflies on material containing leishmania. The material consists of the plasm obtained by defibrinating and centrifuging the blood of a hamster mixed with the broken up spleen of an infected hamster. Before use the mixture is centrifuged to throw down coarse particles and sufficient red blood corpuscles added to give the concentration in blood. With the mixture, which contains large numbers of leishmania a circular piece of flannel is infiltrated and this placed on a shallow dish is covered with a piece of hamster skin from which the muscular layer on one surface and the hair on the other have been removed. The skin is stretched tightly over the flannel and tied down. This arrangement is placed on an electrically heated plate which is kept at a uniform temperature of 35° C. A small cage containing about 20 sand flies is inverted over the skin and the whole covered to exclude light. In thirty minutes 95 per cent. of the flies will have fed. Flies fed by this method never die within three or four days. If they are kept in an ice box at 21° C. and refed they will live much longer, even as much as eighteen days. From July 16th to August 31st, 1928, 1,918 *Phlebotomus major* and 213 *P. sergenti* were fed satisfactorily in this manner.

C. M. W.

Hu (C. H.), Huie (Dorothy) & Lee (C. U.). **Slapping as a Factor in Transmission of Kala-Azar by Sandflies (Phlebotomus).**—*Proc. Soc. Experim. Biol. & Med.* 1929. Jan. Vol. 26. No. 4. pp. 280–284. With 1 text fig. [3 refs.] [Peking Union Med. College, Peking, China.]

Sandflies which have become infected as a result of ingestion of leishmania were allowed to feed on pieces of sterile flannel soaked in blood mixture. While feeding they were crushed on the flannel by a specially devised " slapper " worked by a spring. After the flies were crushed cultures were made from the flannel. In one instance a culture of leishmania was obtained. It is suggested that infection may occur in nature by the crushing of sand flies on the skin.

C. M. W.

TIMPANO (P.). Un caso di kala-azar, complicato da poliomielite anteriore acuta, con esito in guarigione spontanea. [**Case of Kala Azar which recovered after Acute Anterior Poliomyelitis.**]—*Policlinico.* Sez. Prat. 1929. May 27. Vol. 36. No. 21. pp. 741–742.

A child aged 2 years and 7 months suffered from fever and enlargement of the spleen. As it came from a malarial district it was treated with quinine. Eventually, a spleen puncture revealed numerous leishmania and a diagnosis of kala azar was made. Though antimony treatment was advised this was not carried out. Later, the child was attacked by acute anterior poliomielitis. Without any treatment whatever a complete recovery was made. The author states that this is the second case of spontaneous recovery from kala azar which has come under his notice.

C. M. W.

BISSET (W.). **A Case of Kala-Azar.**—*Jl. Roy. Army Med. Corps.* 1929. Feb. Vol. 52. No. 2. pp. 131–132.

The case recorded is one of a British soldier admitted to hospital at Lebong (India) for tuberculosis of the tracheo-bronchial glands, a diagnosis which appeared to be confirmed by X-ray examination. Extraction of two teeth was followed by extensive cancrum oris. Kala azar was suspected when a blood-count showed 40 per cent. of lymphocytes and 20 per cent. of large mononuclears and a strongly positive aldehyde test. Owing to the sensitiveness of the patient it was not possible to puncture the spleen. A course of urea stibamine resulted in the arrest of the disease, the patient being discharged pending "change to England," after having 3·15 grams of the drug. It is noteworthy that the spleen was never more than two finger-breadth's below the costal margin, and that there was no obvious double remission of the temperature. Though all the more important complications associated with kala azar were present, under specific treatment a rapid recovery was made, the patient being able to be on his feet twenty-eight days after treatment was commenced.

C. M. W.

GHOSH (Nisanath). **An Unusual Complication of Kala-Azar.**—*Indian Med. Gaz.* 1929. Apr. Vol. 64. No. 4. p. 205.

A Mohammedan aged 24, who was undergoing treatment with urea-stibamine, injured his scrotum with a bamboo. The trifling scratch led to ulceration and ultimate gangrene which appeared to result from the patient's neglect of cleanliness. Though one testis became exposed the patient ultimately recovered completely.

C. M. W.

NAPIER (L. Everard). **The Pentavalent Compounds of Antimony in the Treatment of Kala-Azar. Part IV. Urea-Stibamine: an Analysis of the Treatment in 70 Consecutive Cases. Part V. Stibamine Glucoside (Neostam): an Analysis of the Treatment in 57 Consecutive Cases.**—*Indian Jl. Med. Res.* 1929. Apr. Vol. 16. No. 4. pp. 901–910. [6 refs.]; 911–919. [5 refs.]

In Part 4 of this paper the author describes the treatment of 70 unselected cases of kala azar with urea stibamine. It is noted that this substance is of relatively low toxicity, though not as low as some other pentavalent compounds of antimony. Different batches have different percentages of antimony, the range being 20 to 44 per cent. In the treatment described three brands of urea stibamine were employed and no batch contained less than 30 per cent. of antimony. Of the 70 cases 64 were discharged as cured, 4 died during treatment and

2 which had resisted previous treatments failed to respond and died subsequently. Injections were made intravenously three times a week till in most cases 10 or 11 doses had been given. In every instance a liver or spleen puncture with culture was carried out before the patient left hospital and 10 days after the last injection. Of the 64 patients discharged as cured accurate information was available for 51. Of these one died after a surgical operation, one relapsed and 49 remained in perfect health for 6 months or more and were thus, according to the author's standard, cured. Of those cured 4 had relapsed after a previous treatment while 45 were treated for the first time. The mean total dose of the drug given to the 49 cured cases was 2·28 gm. Of the 4 cases which had resisted previous treatment the mean dose was 3·23 gm. The mean dose of the 45 cured cases which had received no previous treatment calculated for a 100 lb. bodyweight was 3·0 gm. and for the 4 previously treated cases 4·54. In an Appendix an analysis of 89 cases treated by Dr. FOSTER with the same drug is given. Of these 81 were cured, 4 died, 2 relapsed and 2 gave no history.

The conclusion is that urea stibamine is a drug of very considerable value in the treatment of kala azar.

Part 5 relates to a series of 57 unselected cases of kala azar treated with stibamine glucoside (Neostam). Of these 53 were discharged as cured, 2 were resistant and 2 died during the course. The two resistant cases had already proved resistant to other drugs. The two patients who died were both very debilitated when admitted. Of the 53 cases discharged as cured the subsequent history of 44 is known. Of these 9 relapsed and 35 remained in good health. The mean total dose of the drug given to the 35 cured cases was 2·14 gm. or, calculated per 100 lb. of body weight, 3·17 gm. The dose per 100 lb. of body-weight according to age was under 10, 4·13 gm., 10 to 20, 3·25 gm., over 20, 2·48 gm. Thus there was a tendency to give the younger patients a relatively larger dose and it is noted that the relapse rate was lowest among them. The drug was administered intravenously, in the first few cases in a 4 per cent. solution and in the others in a 5 per cent. solution. About two-thirds of the previously untreated cases received in all ten injections. The initial dose was usually 0·1 gm. and the maximum 0·3 gm. It is concluded that stibamine glucoside is a drug of considerable value in the treatment of kala azar.

C. M. W.

LLOYD (R. B.), NAPIER (L. Everard) & PAUL (S. N.). **The Serological Control of Treatment of Kala-Azar with Observations on the Significance of Hypoproteinaemia.**—*Indian Jl. Med. Res.* 1929. Apr. Vol. 16. No. 4. pp. 1065–1098. With 21 graphs. [4 refs.]

In a previous paper (*ante*, p. 319) reference was made to the protein graph in kala azar and it was suggested that it might be used as a serological control of the progress of treatment as the Wassermann reaction is used in syphilis. In the present paper 21 graphs are reproduced and discussed and the authors feel justified in making certain generalizations. The graphs strongly support the view that the changes they indicate may be used as a control of treatment as previously suggested. It has been proved that the serum proteins reach their normal proportions in approximately 120 days from the commencement

of treatment, no matter what may have been the kind or amount of antimony treatment given. When this stage has been reached the case is said to be in a condition of serological cure. The typical graph (*loc. cit*, p. 320) shows that there are two stages. In the first there is a rapid rise in the amount of albumin and a fall in that of the globulin, so that the albumin and globulin lines cross one another. At the same time examination of the globulin for its two constituents euglobulin and pseudoglobulin reveals the fact that there is a steady fall of the former while the latter, forming at first more than half the total globulin, falls below the euglobulin and then rises above it so that its line crosses that of the euglobulin twice. When these changes have occurred the second stage commences, when it will be found that the albumin and total globulin quickly reach the normal level while the pseudoglobulin continues steadily to increase and the euglobulin to decrease till at about the 120th day they are present in normal proportions and serological cure is reached. The authors are of opinion that the speed of onset of the second stage may be regarded as an index of the potency of the treatment employed. It is much more rapid when concentrated courses of 693 B are employed than under any other mode of treatment (*loc. cit*, p. 321). It is noteworthy that when serological cure has been reached the formol-leucogel reaction has become negative.

The impression has been gained by one of the authors (L. E. N.) that cases of moderate duration in which there is high total globulin and euglobulin and a strongly positive formol-leucogel reaction respond better to treatment than those of short history. It would seem, therefore, that the protein changes so characteristic of well-established cases may be of the nature of an immunity response which assists them towards a cure when treatment is commenced. It has been noted that parasites may still be present after a course of treatment but that their presence is no indication that relapse would necessarily occur. It has been found that immediately after the concentrated eight-day course of 693 B, which produces a very high percentage cure rate, parasites are almost always present, but that if examination of the spleen for parasites is delayed the longer the interval the smaller are the chances of finding parasites.

The suggestion is put forward that the predisposing cause of infection with the parasite of kala azar is in some way connected with the reduction of the albumin content of the serum. In malaria the albumin is greatly reduced and the globulin slightly reduced. Under quinine treatment both curves rapidly rise to normal. If kala azar supervenes on a malarial infection the globulin curve rises above normal and the malarial parasites disappear from the blood. It is very seldom that malarial parasites are found in the blood in kala azar but when antimony treatment has taken effect typical malarial attacks are common. It would seem that both parasites exist when there is a low total protein content of the serum and that the low albumin is maintained by both parasites but that the increase of globulin in kala azar is unfavourable to the malarial parasite. Typhoid, like malaria, is associated with low protein content and these diseases may be predisposing causes of invasion of the body by the parasites of kala azar.

In secondary syphilis treated with organic arsenicals graphs similar to those of kala azar are obtained and an explanation of the beneficial effect of malaria on metasyphilis may be found in an antagonism between the low albumin type of serum in malaria and the high globulin type of cerebro-spinal fluid in metasyphilis.

The method by which the graphs may be applied to the treatment of cases of kala azar, their variation in resistant cases of the disease and many other details are fully discussed in the paper. It is not possible to deal adequately with these in a summary and those who are interested will be well advised to read the original paper, which is full of information and interesting suggestions.

C. M. W.

CHOPRA (R. N.) & CHOUDHURY (S. G.). **On the Causation of Formol-Gel Reaction in Kala-Azar. Part I.**—*Indian Jl. Med. Res.* 1929. Apr. Vol. 16. No. 4. pp. 925–938. With 1 graph in text. [11 refs.] [Calcutta School of Trop. Med. & Hyg., Calcutta.]

The results of the investigations described show that for any particular kala azar serum there is a definite pH at which the time required for gelation and complete opacity after the addition of formalin is a minimum. If the pH is altered towards the alkaline side it is found that the rate of decrease of opacity is much greater than that of the gelation, while the reverse is the case when the alteration is towards the acid side. If the serum is diluted with an equal volume of conductivity water or physiological saline the gelation is retarded. In diluted sera gelation may occur before or after opacity has developed. These facts suggest that the two processes, gelation and development of opacity, are caused by two different proteins or that formalin reacting with euglobulin produces a marked change in its nature.

C. M. W.

PARADISO (F.). Sulla possibilità di estendere la prova di d'Amato alla diagnosi di kala-azar infantile. [**Possible Extension of Amato's Test to the Diagnosis of Kala Azar.**]—*Pediatria.* 1929. June 1. Vol. 37. No. 11. pp. 596–603. [11 refs.] [Inst. Clin. Pediatrics, Univ., Milan.]

The reaction of Amato is the occurrence of leucopenia shortly after the injection of small doses of antagonistic substances, such as tuberculin in tuberculosis, antisyphilitic drugs in syphilis, homologous vaccines in enteric, etc. The author attempted to obtain this reaction in infantile kala azar by injecting intravenously small doses of tartar emetic. As a result of observations on twenty cases it was found that the naturally occurring leucopenia obscured the results and rendered the reaction of Amato unsuitable as an aid to the diagnosis of kala azar.

C. M. W.

LABERNADIE (V.) & LAFFITTE (N.). Une réserve sur la valeur de la réaction de Chopra et Gupta (kala-zaar). [**Reservation on the Value of the Chopra and Gupta Reaction.**]—*Bull. Soc. Path. Exot.* 1929. Feb. 13. Vol. 22. No. 2. pp. 77–80. [5 refs.] [Colonial Hosp., Pondicherry.]

The authors draw attention to the fact that the antimony reaction of the serum for the diagnosis of kala azar may be misleading if the patient has quinine in the blood. They advise testing the urine by Tanret's reagent to exclude the presence of quinine before the test is made.

C. M. W.

KEIGELUCHIS (I.). [Zur Frage der Züchtung der Leischmanien auf dem festen Nährboden.] [**Culture of Leishmania on Solid Media.**]—*Nachrichten d. Tropischen Medizin.* Tiflis. 1928. Nov. Vol. 1. No. 1. [In Georgian. German summary p. 114.]

While cultivating leishmania on solid medium according to the technique of MAYER and RAY (this *Bulletin*, Vol. 25, p. 859) the author found that by using Legroux test tubes instead of Petri dishes, better and purer cultures were obtained. Further, the use of sublimate solution which the employment of Petri dishes involves was no longer necessary.

C. M. W.

BUSS (G.). Untersuchungen mit Leishmania-Vakzine. [**Experiments with Leishmania Vaccine.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1929. Feb. Vol. 33. No. 2. pp. 65–83. With 3 text figs. [11 refs.] [Kaiser-Wilhelm Society for the Advancement of Science, Sao Paulo.]

The paper describes experiments designed to test the reaction of the skin in cases of S. American leishmaniasis, when a vaccine of cultural forms of the causative organism is injected. WAGENER (this *Bulletin*, Vol. 22, p. 202) first noted that such a skin reaction occurred in immunized rabbits, while MONTENEGRO (*l.c.*, Vol. 23, p. 585) applied it to human beings suffering from the disease. The paper under review is a further contribution to the subject. The author employed an antigen consisting of cultural forms of leishmania from a medium which was the same as Noguchi's semi-solid agar, except that 0·5 per cent. dextrose was added to the physiological saline used. After ten to twelve days growth at room temperature, there was a culture layer at the top of the tube, 3 to 6 mm. in thickness. This was removed by a pipette and the flagellates washed by centrifuging in saline solution three of four times. The final suspension was made by adding saline solution alone and heating to 60° C. for an hour on two successive days, saline solution with 0·5 per cent. phenol and heating to 60° C. for an hour on one day, or saline solution with 0·5 per cent. formol and keeping in the incubator at 37° C. for three days. Sterility of the antigen was tested by culture methods. After trial it was found that the best results were obtained with an antigen containing one to three million organisms per cubic centimeter and phenol as the sterilizing agent, for the formol was liable to cause pain on injection. The results obtained were similar to those recorded by MONTENEGRO. When 0·1 cc. of the antigen is injected into the skin of a patient suffering from cutaneous leishmaniasis, there develops in 48 hours a definite palpable papule which can easily be detected on account of its firmness even in dark skinned individuals in whom redness of the skin cannot be seen. The papule persists for 4 to 5 days and then quickly disappears As control was employed the diluting fluid containing some of the culture medium. This on account of the traces of agar and serum produces a small papule, which, however, in 48 hours reaches its maximum development and quickly disappears. In addition to two strains of Brazilian leishmania isolated by the author, two strains of *Leishmania tropica* and one of *L. donovani* were employed for preparation of antigen. Any one of these antigens gave the same reaction so that there is no specificity as regards the species. In thirty undoubted cases of cutaneous leishmaniasis a definitely positive reaction occurred, while of three doubtful cases two gave a very probable positive result, and one a definitely positive one. In ten controls it was definitely negative in

eight and doubtful in two. It is evident the test will be of use in the diagnosis of obscure cases. As a curative agent the antigen did not give satisfactory results.

C. M. W.

PARROT (L.). Sur la contagion directe du bouton d'Orient. [**Direct Contagion of Oriental Sore.**]—*C.R. Soc. Biol.* 1929. Feb. 22. Vol. 100. No. 7. pp. 467–468. [4 refs.] [Pasteur Inst. of Algeria, Algiers.]

Though it is generally admitted that oriental sore is transmitted by sand flies, some still believe that direct infection from case to case may occur. The parasite, being a motionless body, is not adapted to active penetration of the skin, so that if such infections occur they must be the result of parasites being transferred to abrasions. If this happened with any frequency it would be expected that cases would occur throughout the year, whereas there is a definite seasonal incidence. Furthermore, the sores would occur most usually on the back of the hand and fingers, where abrasions are most common. Of 249 sores observed in Algeria only 9 occurred in these situations. Furthermore, the sores are generally covered by a scab which hinders the escape of parasites and when pus exudes this is contaminated with bacteria, and leishmania cannot be found in it. Practically all the cases of oriental sore which have been recorded as resulting from direct contagion have occurred in places where sand flies are common. For these and other reasons it is evident that the contaminative method of infection in oriental sore has not been established.

C. M. W.

ADLER (S.) & THEODOR (O.). **Attempts to transmit** *Leishmania tropica* **by Bite: the Transmission of** *L. tropica* **by** *Phlebotomus sergenti.*—*Ann. Trop. Med. & Parasit.* 1929. Apr. 26. Vol. 23. No. 1. pp. 1–18. With 1 plate. [7 refs.] [Microbiol. Inst., Hebrew Univ., Jerusalem.]

The authors note that they have shown previously that *L. tropica* is a natural flagellate of *Phlebotomus papatasii* and that the flagellates from naturally infected flies and flies artificially infected from sores or cultures are infective when inoculated into the skin of man. It is pointed out that human beings not previously infected may show a natural immunity, for of two inoculated nearly two years ago with parasites from a cutaneous lesion, only one has developed an infection. Of nineteen volunteers inoculated with flagellates from artificially infected sand flies, only six developed oriental sore. It is further noted that strains of *L. tropica* vary in their infectivity to sand flies. Thus, one from the Syrian village, Bar Elias, where during the last six years almost every inhabitant has contracted the disease, is highly infective to the sand fly. On the other hand, a strain from Jericho, where the disease is comparatively rare, is much less infective to the fly. Sand flies infected by feeding on cultures of *L. tropica* through a rabbit skin membrane, were fed on twelve volunteers and one puppy. The number fed on each case varied from 2 to 88. A negative result was obtained in every one except volunteer No. 2, in which after a period of ten months, lesions appeared on the left arm at the site on which the flies had fed. The lesions were in the form of two small vesicles which were followed a day later by the appearance of two more. Fluid from the vesicles

contained extra-cellular parasites. The authors are reluctant to conclude that this experiment affords the final proof of sand fly transmission of oriental sore, for after the experiment the volunteer lived in a quarter of Jerusalem where there are always a number of imported cases of oriental sore. Furthermore, about six months after the infected sand flies had fed on the left arm, as no infection appeared to have occurred, the volunteer (as in the case of Nos. 1, 6 and 8) was used for other experiments. Cultures were inoculated into two points on the lower part of the left arm, while later, flagellates from infected *Phlebotomus sergenti* were inoculated into three scarified points on the right arm, and still later into two points in the left deltoid region. No infection had resulted from the first of these inoculations in five months, nor from the third in four months, but a little over three months after the second and eleven days after the appearance of the vesicles referred to above, a raised spot containing parasites appeared at one of the inoculation points on the right arm. It is unfortunate that the first experiment was complicated by subsequent inoculations and the possible exposure to natural infection, but it would seem that the appearance of the vesicles on the small area, about one inch square on which the sand flies had fed, leaves little room for doubt that the infection had occurred as a result of the feeding of the infected insects.

It is pointed out that *Leishmania tropica* develops in *Phlebotomus sergenti* as it does in *P. papatasii*. In both flies, however, only a small proportion of the sand flies acquire a proboscis infection if they have been kept at a temperature of 19° C. to 23° C. At higher temperatures (27° to 30° C.) proboscis infections in *P. papatasii* are much commoner and it is suggested that this may account for the difficulty in producing infections by the bite of infected sand flies, for those fed on the volunteers were kept at the lower temperature. A description of the experiments which demonstrated that flagellates are inoculated into fluid when infected sand flies feed through a rabbit skin membrane is given. The specimens of *P. sergenti* used in the experiments were bred from eggs brought to Palestine from Bagdad in which place one naturally infected sand fly of this species was encountered. The flagellates from this fly were inoculated into volunteer No. 8, but no infection had resulted in seven months.

C. M. W.

ADLER (S.) & THEODOR (O.). **Additional Evidence on the Occurrence of *L. tropica* in Wild *Phlebotomus papatasii*.**—*Ann. Trop. Med. & Parasit.* 1929. Apr. 26. Vol. 23. No. 1. pp. 19–21. [5 refs.] [Microbiol. Inst., Hebrew Univ., Jerusalem.]

The authors previously recorded the fact that three human beings were infected with *Leishmania tropica* by the inoculation of flagellates taken from dissected *Phlebotomus papatasii*. SINTON criticised the diagnosis of the fly, while KNOWLES implied that it was probably *P. sergenti*, owing to the failure in India to infect *P. papatasii* by allowing it to feed on an oriental sore. It is admitted that there might be a fallacy in the diagnosis of the female sand fly, for the value of the characters of the pharynx was discovered later. Nevertheless, the authors note that though LAROUSSE recorded *P. sergenti* in Palestine in 1924, they themselves, in four and a half years' collecting and breeding, during which many thousands of sand flies have been examined, have not encountered a single specimen of *P. sergenti*. It

is now reported that when the three original naturally infected sand flies were dissected, the head of one was mounted and kept. A re-examination of this head reveals the fact that its pharyngeal characters are typical of *P. papatasii.*

C. M. W.

D'UTRA (O.) & SILVA. Quelques caractères des leishmanioses tégumentaires brésiliennes. [**Characters of Dermal Leishmaniasis in Brazil.**]—*Bull. Soc. Path. Exot.* 1928. Dec. 12. Vol. 21. No. 10. p. 846.

On the occasion of the regrettable death of Gaspar VIANNA the author pays a tribute to this investigator in pointing out that the tartar emetic treatment for Brazilian leishmaniasis, first advocated by him, is the one which should be employed for this disease which is not a local infection capable of being dealt with by local measures. It is a general infection, parasites occurring far from the original focus, and on this account demands a general treatment.

C. M. W.

ESCOMEL (E.). La leishmaniose américaine et les leishmanioses en Amérique. [**American Leishmaniasis and Leishmaniases in America.**]—*Bull. Soc. Path. Exot.* 1929. Jan. 9. Vol. 22. No. 1. pp. 35–46. With 12 figs. on 8 plates. [1 ref.]

The author maintains that there are two distinct types of mucocutaneous leishmaniasis in America and that both of them are distinct from oriental sore. American leishmaniasis occurs in Mexico, Central America, and South America, in Colombia, Venezuela, the Guianas, Ecuador, Peru, Brazil, Bolivia, Paraguay, Northern Argentine and Uraguay. It was thought at one time that many of the vases (huacos) made by the Incas which depicted mutilated faces of human beings were based on the deformities produced by the disease. The archeologist Victor LARCO HERRERA has, however, discovered a ceramic illustrating an individual in the act of removing the lips of another person with a cutting instrument (tumis). It seems clear that the pre-Columbian artists in their vases were illustrating the effects of this operation rather than the ravages of disease. The author, however, states that the Incas knew of the disease, for Dr. RIBERO has shown him a vase on which the face shows the typical nasal deformities produced by leishmanial ulceration. The author passes on to a discussion of the differences which exist between oriental sore and American leishmaniasis. The chief of these are the benign character and rapid healing of the former followed by immunity, and the tendency to involvement of the mucosae, the long duration and lack of immunity in the latter. As regards the American disease two distinct types exist. In the one, Uta, the infection is essentially one of the skin, the mucosae becoming involved by direct extension of the ulcerative process; in the other, Espundia, there is a primary skin lesion, but the mucosae become secondarily infected as in syphilis. True oriental sore may be met with in S. America in immigrants from endemic centres of this disease. The S. American disease shows various clinical types; of the cutaneous forms there are the ulcerative, papulo-tuberculous, crusted, lymphangitic and circinate varieties, and of the mucosal forms there are those due to the extension of the cutaneous ulcer of Uta and the secondary ulcerations of Espundia.

The lesions due to leishmania infection are readily confused with others due to blastomycosis—caused by *Cryptococcus americanus.* In many cases the differentiation can be made only in the laboratory. When the two infections co-exist in the same individual the diagnosis is very difficult. Frequently, the response to antimony treatment may be the only indication that the disease is leishmaniasis and not blastomycosis. As regards treatment it is necessary to commence this as early as possible and while giving intravenous injections to destroy all suspicious lesions. Local cauterization, intravenous tartar emetic, and iodine bismuthate of quinine are the best known remedies. Radium, X-rays, diathermy and ultra-violet rays are being used experimentally at the present time.

C. M. W.

DEY (Nepal Chandra). **A Case of Post-Kala-Azar Dermal Leishmaniasis.**—*Indian Med. Gaz.* 1929. Mar. Vol. 64. No. 3. pp. 147–148.

A Hindu boy aged twelve, four months after having been discharged as cured from kala azar, noted small depigmented spots on the lips, chin, arms, legs and body. These increased in size and on the lips, back of wrists, dorsum of feet, anterior aspect of the knee and inner aspect of the elbow were replaced by nodules. Smears made from the cut surface of a nodule revealed leishmania. The spleen was not palpable and the aldehyde test negative. The urea stibamine or antimony test was positive. A course of urea stibamine was commenced and a complete cure resulted after 2·4 grams had been administered. This condition, though fairly common in Calcutta, is rare in Assam where the disease was contracted. The author notes that during four and a half years experience of kala azar in the most heavily infected areas of Nowgong he has seen no other case of the kind.

C. M. W.

ARTAMONOW (A. S.). [Ein Fall von Hautleishmaniose nach einer ueberstandenen inneren Leishmaniose.] [**Dermal Leishmaniasis following Visceral Leishmaniasis.**]—*Russian Jl. Trop. Med.* 1929. Vol. 7. No. 1. pp. 1–3. With 2 figs. on 1 plate. [3 refs.] [In Russian. German summary p. 3.]

A child, seven years of age, contracted kala azar in Kokand in Turkestan. Treatment was commenced in March and complete cure was considered to have taken place by May. In July a sore appeared on the leg and this was diagnosed as oriental sore. There was no recurrence of the kala azar and treatment of the sore effected a cure by October. It is concluded that kala azar does not confer immunity against oriental sore. However, the possibility of a simultaneous or nearly simultaneous infection with both diseases is not ruled out. The author mentions another case in which after recovery from oriental sore kala azar was contracted.

C. M. W.

DOUCAS (Chr.). Cent deux boutons d'Orient sur un même malade. [**Hundred and Two Oriental Sores in One Patient.**]—*Bull. Soc. Française Dermat. et Syph.* 1929. May. No. 5. pp. 469–475. With 2 text figs.

A youth 18 years of age, an inhabitant of Crete, presented himself at Athens for multiple skin lesions which had been diagnosed as of syphilitic origin and had failed to respond to antisyphilitic treatment. The disease commenced as a small papule on the right cheek. Later, other similar papules appeared on various parts of the head and finally on the back of the hands and forearms. In six months there were present in all 102 lesions varying in size from that of a lentil to a two franc piece. A diagnosis of

oriental sore was made by discovery of the parasite in many of the lesions and a complete cure was effected in four and a half months by the injection into the base of all the lesions of solution of emetine hydrochloride.

C. M. W.

VIGNE (P.) & BOURRET (M.). Bouton d'Orient de la face. [**Oriental Sore of the Face.**]—*Marseille-Méd.* 1929. Feb. 25. Vol. 66. No. 6. pp. 310–311.

The patient aged 45 was born in Cesarea in Turkey and lived there all her life till she came to Marseilles where she has been for four and a half years. Six months ago a small papule appeared on the nose and this developed into a typical oriental sore. It was not possible to trace any source of infection in Marseilles, yet the otherwise excessively long incubation period seems to indicate that the disease must have been contracted there. The author recalls that a year ago he had a similar case in a child which had lived in Marseilles two and a half years.

C. M. W.

GUPTA (B. M. Das) & DIKSHIT (B. B.). **Berberine in the Treatment of Oriental Sore.**—*Indian Med. Gaz.* 1929. Feb. Vol. 64. No. 2. pp. 67–70. [4 refs.] [School of Trop. Med. & Hyg., Calcutta.]

Berberine sulphate promises to be a specific cure for oriental sore, for given by infiltrating the tissues around the edge of the sore it brings about complete cure in two to three weeks. Treatment is carried out by injecting 1 to 2 cc. of a 1 per cent. solution of the sulphate or 1 cc. of a 2 per cent. solution of the acid sulphate, the exact quantity depending on the size of the sore. The quantity used on each sore is not injected at one, but at four or more points round the sore. The injections are repeated in a week and again if necessary. The solutions are very stable and can be preserved in sterile tubes with rubber caps, desired amounts being withdrawn by the syringe when required. Tested on cultures of *Leishmania tropica* it was found that in dilutions of 1 in 80,000 inhibition of growth occurred.

C. M. W.

HAMILTON-BROWNE (E.). **Oriental Sore.**—*Jl. Assoc. Med. Women in India.* 1929. Feb. Vol. 17. No. 1. pp. 8–11.
DEVI (Lakhsmi). **Oriental Sore Treatment.**—*Ibid.* pp. 11–16.

The paper refers to the frequency of oriental sore in Lahore and advocates treatment by the berberine sulphate method of VARMA and CHANDANI which leads the author to write, " we have had great success in its use." The treatment is carried out as follows. A quarter of a grain of berberine sulphate is dissolved in 1·5 cc. of distilled water and sterilized. The solution is injected round the sore. The needle is inserted subcutaneously, half an inch from the margin of the sore and passed forward till it reaches the margin of the ulcer when 0·5 cc. is injected. The procedure is repeated at two other points. If the sore is not healed in a week the treatment is repeated. Rarely is a third treatment necessary.

C. M. W.

DEVI (A. Lakshmi). **Berberine Sulphate in Oriental Sore.**—*Indian Med. Gaz.* 1929. Mar. Vol. 64. No. 3. pp. 139–140.

Details of the treatment of twelve cases of oriental sore in Lahore by local injections of berberine sulphate are given in the paper. Of the 18 sores in the 12 cases, 6 healed completely with one injection, 5 with two, five with three and 1 in which the original diagnosis was doubtful, did not show any improvement. One case did not return after the first injection. In the treatment the margin of the sore is infiltrated with a 2 per cent. solution of the drug. In most of the cases 1·5 cc. was injected at each treatment.

C. M. W.

FUCHS (David). A proposito de um caso de leishmaniose tegumentar. [**A Case of Dermal Leishmaniasis.**]—*Brasil-Medico.* 1929. Jan. 12. Vol. 43. No. 2. pp. 46–51. With 3 text figs.

A typical case of mucocutaneous leishmaniasis which was cured by intramuscular injections of antimosan and local applications of a paste containing stibosan, leads the author to write a general review of our knowledge of this disease.

C. M. W.

MAYER (Martin). Tierversuche mit *Leishmania tropica* (Orientbeule). [**Animal Experiments with** *L. tropica.*]—*Dermat. Woch.* 1929. Feb. 23. Vol. 88. No. 8. pp. 286–288. With 3 text figs. [Inst. for Ship & Trop. Diseases, Hamburg.]

The author notes that he has already shown that the European hamster, *Cricetulus frumentarius,* is as susceptible as the Chinese species, *Cricetulus griseus,* to infection with *Leishmania donovani.* The observations of CASH and HU that Chinese hamsters infected with this parasite frequently showed massive infection of the reticulo-endothelial system of the skin, led the author to examine his infected European hamsters. In them he found the skin heavily infected. Usually there was no visible change in the skin, but sometimes there were small excoriations on the abdomen and these revealed parasites in large numbers.

European hamsters were inoculated intraperitoneally with cultures of *Leishmania tropica* with a view to finding out if in them a generalized infection, like that produced by *L. donovani,* would occur. Strains from Palestine, Turkestan and S. America were used. Only on one occasion was a generalized infection produced. Kala azar hamsters were inoculated in the skin of the abdomen with cultures of the organisms of kala azar and oriental sore. In both cases after two or three weeks a black discoloration of the skin, having the appearance of haemorrhage, at the site of inoculation was observed. On section it was seen that the dark colour was not due to parasites which were deep in the tissue, but to the new formation of hair follicles which were closely packed together in the reduced fat tissue. Inoculation into the skin of the nose, ears and tail, produced local infections. On the ear and nose swellings without ulceration were produced, and parasites could be recovered after many months. One of the hamsters inoculated in the skin of the ear with the Palestine strain showed swelling with crust formation. On removal of the crust fluid was obtained containing many *L. tropica.* Two other hamsters inoculated subcutaneously at

the root of the tail developed ulcers heavily infected with leishmania. From these observations it appears evident that the hamster is not such a suitable experimental animal for oriental sore as it is for kala azar.

C. M. W.

PARROT (L.). De la virulence des cultures de *Leishmania tropica* pour la souris blanche. [**Virulence of** *L. tropica* **Cultures for the White Mouse.**]—*C.R. Soc. Biol.* 1929. Feb. 1. Vol. 100. No. 4. pp. 238–239. [2 refs.] [Pasteur Inst., Algiers.]

The author in collaboration with DONATIEN (this *Bulletin*, Vol. 24, 647) showed that mice inoculated in the skin of the tail developed local lesions resembling oriental sore. The lesions persist often for a year and parasites are constantly found in them. The author emphasizes the use of this, not only for maintaining strains, but for the recovery of cultures which have been lost through contamination or other cause. Mice inoculated at intervals of about a month, will yield material whenever it is required for experiment or demonstration.

C. M. W.

PARROT (L.). Sur la conservation du virus du bouton d'Orient chez la souris blanche. [**Preservation of Virus of Oriental Sore in White Mice.**]—*C.R. Soc. Biol.* 1929. Feb. 1. Vol. 100. No. 4. pp. 239–240. [1 ref.] [Pasteur Inst., Algiers.]

The author having isolated seven strains of *Leishmania tropica* from cases of oriental sore, found that at first they regularly infected mice, whether injected intraperitoneally or into the testis or skin of the tail. The last method of inoculation produced a local lesion, resembling oriental sore in man, but the others gave rise to generalized infections, as manifested by cutaneous localizations of the parasites, ulceration of the ears, tail and scrotum, adenitis and periarthritis, and hypertrophy of the spleen. Three of these cultures were maintained by subculture, during which the virulence has appreciably diminished. After periods of subculture of two months to a year, two of the strains failed entirely to infect mice. The other strain maintained for 24 months, failed to infect by the intraperitoneal method, though at ten months it infected intratesticularly. These observations indicated that in judging of the virulence of strains of leishmania, the length of time of subculture has to be taken into account. A virus which has been kept by subculture and fails to infect mice is not necessarily different from one which is still infective.

C. M. W.

PARROT (L.). Sur la vaccination contre le bouton d'Orient. [**Vaccination against Oriental Sore.**]—*C.R. Soc. Biol.* 1929. Feb. 15. Vol. 100. No. 6. pp. 411–412. [2 refs.] [Pasteur Inst., Algiers.]

Attempts were made to vaccinate monkeys (*Macacus inuus*) against oriental sore by use of a vaccine prepared from *Leishmania tropica* obtained from the testicular infection in mice. Neither this procedure nor the injection of living parasites from mice or avirulent cultures produced any immunity.

C. M. W.

DONATIEN (A.) & LESTOQUARD (F.). La leishmaniose viscérale du chien. [**Canine Kala Azar.**]—*Rev. Vét. et Jl. de Méd. Vét.* 1929. Mar. Vol. 81. pp. 117–135. With 2 text figs. [8 refs.] [Pasteur Inst., Algiers.]

This is a general account of canine kala azar and is chiefly a summary of work published on the subject. For dogs suffering from the disease intravenous injections of tartar emetic are advised, commencing with a dose of 1 centigram in 1 per cent. solution and increasing to a maximum of 5 centigrams. Injections are given on alternate days till four injections have been made. After a week's rest the course of four doses is repeated. In some cases two courses will effect a cure ; in others more are required.

C. M. W.

DONATIEN (A.), LESTOQUARD (F.) & PARROT (L.). Parasitisme anormal dans un cas de leishmaniose du chien. [**Abnormal Parasite Distribution in a Case of Canine Leishmaniasis.**]—*Bull. Soc. Path. Exot.* 1929. Apr. 10. Vol. 22. No. 4. pp. 252–253. [Pasteur Inst., Algiers.]

A dog showing all the symptoms of canine kala azar was brought from the pound to the Pasteur Institute in Algiers. It was noted that there were scabbed ulcers on the ears, legs and abdomen, unilateral keratitis and patches on the body from which the fur had disappeared. The serum solidified with formol (20 grams of serum +2 grams of formol) in 22 minutes. Leishmania were found in the ulcers on the legs, ears and abdomen. Splenectomy was performed and contrary to expectations the organ was small and contained few parasites. The dog died a few days later. Parasites were scanty in the bone marrow, very scanty in the glands, but more numerous in the liver. This dog was anomalous, therefore, in having more parasites in the skin than in the internal organs. The authors remark that this condition has not been observed previously, but there is evidently some resemblance to that described by CHODUKIN and SCHEWTSCHENKO in Tashkent (*ante*, p. 323).

C. M. W.

SOFFIEWE (M. S.) & SCHÉWTSCHÉNKO (Ph. J.). [La vitalité de la *L. canis* dans l'appareil digéstif du *Phlebotomus papatassii* (Scop).] [**Survival of** *L. canis* **in** *P. papatasii.*]—*Pensée Méd. d' Usbékistane.* Tashkent. 1929. No. 5. pp. 48–55. With 37 figs. [In Russian. French summary p. 100.]

The paper describes experiments with *Phlebotomus papatasii* and cutaneous leishmaniasis of dogs in Tashkent. They were carried out as described by KHODUKIN (*ante*, p. 324) and like this observer the authors obtained infection of the flies. Wild sand flies were chiefly employed and after feeding on the sores they were kept at a temperature of 21° to 28° C. and dissected after one to eight days. After one day 25 flies gave a percentage of 96 infected with flagellates, after two days 26 gave 69·2 per cent., after three days 26 gave 61·5 per cent., after four

days 59 gave 20·4 per cent., after five days 52 gave 11·5 per cent., after six days 37 gave 2·7 per cent., after seven days 25 gave 4 per cent., while after eight days 74 gave 4·05 per cent. Thus the percentage of infections in the flies decreased rapidly after the third or fourth day. The flies employed were collected in a locality where no naturally infected flies were found. In a batch of twenty-five flies collected in another locality two were found naturally infected.

C. M. W.

ADLER (S.) & THEODOR (O.). **Observations on** *Leishmania ceramodactyli* **n. sp.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1929. Jan. 30. Vol. 22. No. 4. pp. 343–356. With 16 figs. [11 refs.] [Microbiol. Inst., Hebrew Univ., Jerusalem.]

Interest in *Leishmania tarentolae* was first aroused by the suggestion of SERGENT, LEMAIRE and SENEVET in 1914, that this flagellate was possibly *Leishmania tropica* and that the gecko, *Tarentola mauritanica*, might act as a reservoir for the virus of oriental sore. NICOLLE, BLANC and LANGERON in 1920, compared cultures of the two organisms and concluded that they were different, because they differed in size while *L. tarentolae* did not produce oriental sore when injected into man and monkeys. YOUNG and HERTIG (1928) reported they had produced with *L. tarentolae* infections in hamsters similar to that caused by *L. infantum*, and the reviewer suggested that on this account the gecko might be the reservoir of the virus of Mediterranean kala azar. SHORTT and SWAMINATH (1928) isolated a similar parasite from the gecko, *Hemidactylus* sp. in India, and actually observed leishmania forms in leucocytes in the peripheral blood. While in Bagdad, the writer of the paper under review investigated by heart blood culture the following geckos, *Ceramodactylus doriae*, *Gymnodactylus scaber*, *Alsophylax tuberculata* and *Hemidactylus persicus*. The first named species alone gave cultures of leishmania which were studied in culture and in sand flies. The flagellates differed from cultural forms of various leishmania, including two strains of *L. tarentolae*, by the presence of certain long forms with the body up to 35 μ in length. By feeding sand flies, *Phlebotomus papatasii*, on an infected gecko or on cultures, it was found that development took place with a tendency for the flagellates to take up a position in the hind gut and attach themselves there and not in the stomach and cardia, as occurs with the leishmania which produce disease in man and *L. tarentolae*. Infected sand flies pass flagellates in various stages of development in their faeces. It is concluded that *P. papatasii* is probably the vector of the flagellate and that infection of the gecko takes place by oral contamination. Immune sera, prepared in rabbits from this flagellate and the two strains of *L. tarentolae*, showed that in culture media made with the sera, *L. tarentolae* was agglutinated by its homologous serum, but not with that of the flagellate of Ceramodactylus and vice versa. For the various reasons given above it is concluded that the flagellate of Ceramodactylus represents a new species which is named *Leishmania ceramodactyli* and that it occupies an intermediate position between the purely insect leptomonads and the other species of Leishmania of which the sand fly development is known.

C. M. W.

DAVID (Anna.) Note préliminaire sur un *Leishmania* trouvé chez le lézard gris de la région de Tibériade (Basse-Galilée, Palestine). [**Leishmania found in a Grey Lizard in Lower Galilee.**]—*Ann. Parasit. Humaine et Comparée.* 1929. May 1. Vol. 7. No. 3. pp. 190–192. [Microbiol. Inst., Hebrew Univ., Jerusalem.]

By cultivation of the heart blood of sixteen lizards (*Agama stellio*) in Palestine, the author was able to demonstrate that four of them were infected with leishmania, flagellates of the leptomonas type appearing in the cultures. Examination of the alimentary canal of the lizards did not reveal any intestinal infection, but prolonged blood examinations revealed on one occasion a single mononuclear leucocyte containing sixteen parasites of the typical leishmania form.

C. M. W.

BLOCH (J. I.). [Sur la préparation des cultures de la *L. tropica* pour les vaccins.] —*Pensée Méd. d'Usbékistane.* Tashkent. 1929. No. 5. pp. 90–91. [4 refs.] [In Russian.]

DÍAZ (Navarro). Un caso más de leishmaniosis visceral.—*Medicina Países Cálidos.* Madrid. 1929. Mar. Vol. 2. No. 2. pp. 137–138.

TROPICAL MYCOLOGY.

CASTELLANI (Aldo). **Fungi and Fungous Diseases. Lectures I-III.**—*Arch. Dermat. & Syph.* 1927. Oct.–Dec. Vol. 16. Nos. 4–6. pp. 383–425; 571–604; 714–740. With 45 figs. [16 refs.]; 1928. Jan.–Mar. Vol. 17. Nos. 1–3. pp. 61–97. With 3 figs. [2 refs.]; 194–220. [1 ref.]; 354–379. With 44 figs. (4 coloured plates). [23 refs.]

This series of 6 papers comprises two lectures delivered by the author at the University of Illinois in 1926, each lecture supplying material for three papers. In the first three papers (lecture I) the author gives a general outline of elementary mycology and a general review of classification with special reference to the medical aspect of the subject. In this lecture he also describes the phenomenon which he terms "symbiosis" between bacteria and fungi. The author's method of utilizing the fermentation powers of certain lower fungi for the identification of various carbohydrates, and its application to urine analysis, is also described.

The second lecture, forming the last three papers, deals with fungous diseases. Short accounts of the different mycoses are given, together with lists of the fungi known or suspected to be the causal agents, clinical description, diagnosis, prognosis, treatment, and, in many cases, descriptions of illustrative cases. The first of these three papers deals with internal mycoses, including thrush, stomatitis, bronchomycoses, tonsillomycoses, and mycoses of the nervous system, sensory organs and genito-urinary organs. The last two papers deal with dermatomycoses, including trichomycoses, cryptococcoses, blastomycoses, various tineas, pinta, acladiosis and mycotic pruritus.

P. Tate.

DE MAGALHÂES (Octavio). [In Portuguese & English.] Ensaios de mycologia. **Studies on Mycology.**—*Mem. Inst. Oswaldo Cruz.* 1928. Vol. 21. No. 1. In Portuguese pp. 173–180. With 6 plates. [6 refs.] In English pp. 181–188. With 6 plates. [6 refs.]

In Brazil during 13 months, 6 cases of sporotrichosis were observed, two of them being of animal origin. *Endomyces albicans* was obtained for the first time in Pelatos in a large mouth lesion. Several ringworm fungi were seen, including a new species of *Microsporum* which is described in detail and is named *M. circuluscentrum.*

P. T.

BARONI (Benigno). Sur un milieu de culture pour le développement et la conservation des champignons pathogènes. [**A Culture Medium for Pathogenic Fungi.**]—*C.R. Soc. Biol.* 1929. Apr. 19. Vol. 100. No. 12. pp. 994–995. [5 refs.]

The author finds a medium containing cocoa and cocoa-butter very good for isolating pathogenic fungi such as Actinomyces, Oospora and Sporotrichum; and states that when grown on it they retain their virulence, and that sometimes species which have lost their virulence as

a result of successive sub-culturing on ordinary media regain their virulence when grown on this new medium. It is made as follows :—

Prepare broth with 300 grams of lean beef in 1,000 cc. distilled water ; cool, and filter. Heat the broth and add 5 grams rock salt, 12 grams peptone —Witte or Chapoteaut—18 grams agar. Boil for 10 minutes ; filter warm ; and adjust to a slightly acid reaction. Add 15 grams commercial cocoa and 5 grams of very pure cocoa-butter ; boil for 15 minutes, and filter through gauze. Add 60 grams glucose, mix well, and distribute in tubes. Sterilize at 100° C. for 60 minutes on three successive days.

P. T.

GALLOWAY (David). **The Otomycosis of the Malay Archipelago commonly called "Singapore Ear."**—*Malayan Med. Jl.* 1929. Mar. Vol. 4. No. 1. pp. 3–6.

Otomycosis is very common in the Malay Archipelago and is found in about 70 per cent. of all ear diseases, and mostly affects Europeans. Now the causal fungus is most commonly an Aspergillus—*A. flavus*, *A. niger*, or *A. fumigatus*—but about 30 years ago Mucor was the commonest parasite. The symptoms are deep-seated and persistent pruritus ; varying degrees of deafness ; sensation of moisture in the meatus ; and the extrustion of scaly, membraneous or soapy material from the meatus. In cases where there is trauma of the meatus true inflammation supervenes, and then pain dominates all other symptoms. Treatment consists in the application of dilute or strong antiseptics such as bichloride of mercury, silver nitrate and boric acid, according to whether trauma is present or not, for a few days, and then syringing out the parasite. After-treatment should be prolonged and should consist of daily application of antiseptic preparations.

P. T.

GREEN (Richard). **Notes on a Case of "Black Tongue."**—*Indian Med. Gaz.* 1928. July. Vol. 63. No. 7. pp. 381–384. With 5 text figs. [4 refs.] [Med. Research Inst., Kuala Lumpur, F.M.S.]

The patient, a male European aged 36, had the dorsal surface of the posterior two-thirds of the tongue coated with a moist black fur, but was otherwise healthy. Budding yeast cells were present in scrapings, and cultures of an organism believed to be *Cryptococcus linguae-pilosae* Lucet (1910) were obtained. The condition readily yielded to treatment with Lugol externally, and an alkaline gentian mixture internally.

P. T.

REDAELLI (Piero). Studii sulla Nocardiasi sperimentale. Actinomicosi, Streptotricosi. Parte I. Infezione primaria, basi anatomiche e fattore cellulare della immunità naturale. Parte II. Basi anatomiche e fattore cellulare della immunità acquisita. [**Studies on Experimental Actinomycoses. Part I. Primary Infection and Cellular Factor in Natural Immunity. Part II. Anatomical Basis and Cellular Factor in Acquired Immunity.**—*Bol. d. Istituto Sieroterap. Milanese.* 1928. Feb., Mar. & May. Vol. 7. Nos. 2, 3 & 5. pp. 75–101 ; 121–135. With 8 plates (3 coloured). [21 refs.] English summary p. 134 ; pp. 239–265. [25 refs.] English summary p. 264. [Inst. of Path Anat., Univ., Pavia.]

Using the species *Nocardia* [*Actinomyces*] *sanfelicei* n. sp. (=acid-fast Streptothrix described by SANFELICE 1921) the author studied the

primary infection and cellular factor of natural immunity in receptive animals (guineapigs, rabbits), less receptive animals (dogs), and in refractory animals (fowl).

In less receptive and refractory animals there is a more ready reaction on the part of the organism which results in the rapid exhaustion of the disease in refractory animals, and in the passage of the disease to the chronic state in less receptive animals. Thus, less receptive and refractory animals appear to be more sensitive to the parasite and to have the power of reacting more rapidly.

Repeated small doses of *Nocardia sanfelicei* into receptive animals sometimes induce in them a state of hyper-receptivity and sometimes a state of hyper-resistance. It was not possible to determine why these different conditions were caused in apparently similar animals.

P. T.

LEAO (A. E. de Arêa). Réactions sérologiques dans l'actinomycose (agglutinines, précipitines et fixation du complément). [**Serological Reactions in Actinomycosis.**]—*C.R. Soc. Biol.* 1928. Sept. 18. Vol. 99. No. 26. pp. 878–880. [Oswaldo Cruz Inst., Rio de Janeiro.]

The Actinomyces was isolated from a case of generalized actinomycosis. Cultures on ordinary agar, 15 days old, were triturated and emulsified in physiological salt solution, with the addition of 2 per cent. of formalin. 1 cc. of this emulsion and 1 cc. of diluted serum were incubated at 55° C. for 4 hours and then at 37° C. for 12 hours. Dilutions of 1 in 10 and 1 in 20 gave agglutination which was apparent after 4 hours, and there was distinct agglutination up to a dilution of 1 in 160.

Filtrates of cultures on ordinary broth did not give a precipitans reaction with any dilution of serum or filtrate, starting with 1 in 10.

Two antigens were tried, emulsified cultures in normal salt solution, and filtrates from cultures on ordinary broth. The latter was the better, and gave complete fixation with 0·1 cc. to 0·01 cc. serum. This was a group reaction for other mycoses, especially Coccidioidal granuloma, but it was given in much higher dilutions in cases of actinomycosis.

P. T.

DE LA GUARDIA (Jaime). **A Case of Facial Actinomycosis.**—*Sixteenth Ann. Rep. Med. Dept. United Fruit Company, Boston, Mass.* 1927. pp. 163–165. With 3 text figs. [Preston Hosp., Cuba.]

The subject was a young Cuban woman with good general health. An actinomycotic tumour involved the temporal, maxillary and zygomatic regions, with a central granulomatous ulcer forming the opening of a fistulous tract. Treatment was effective and consisted of excision and curettage of the fistula and granulomatous tissues, and cauterization of the area with pure carbolic acid; followed by dressings with 50 per cent. Lugol and intravenous injection and oral administration of sodium and potassium iodides.

P. T.

BLANC (Georges), CAMINOPETROS (J.) & JOANNIDÈS (Georges). Chronique de l'Actinomycose en Grèce.— [**Actinomycosis in Greece.**]—*Bull. Soc. Path. Exot.* 1928. June 13. Vol. 21. No. 6. pp. 432–435. [Pasteur Inst., Athens.]

Report of 2 cases, both fatal, of pulmonary actinomycosis with cold abscesses, from both of which the *Cohnistreptothrix israeli* was obtained in anaerobic cultures.

W. Jenkins Oliver.

STOVALL (W. D.) & GREELEY (Hugh P.). **Bronchomycosis. Report of Eighteen Cases of Primary Infection in the Lung.**—*Jl. Amer. Med. Assoc.* 1928. Nov. 3. Vol. 91. No. 18. pp. 1346–1351. With 8 text figs. [1 ref.]

Yeast-like fungi identified as "Monilia" were isolated from 18 cases of pulmonary disease, in which they appeared to be primary infections. The clinical aspect varied from mild illness to severe cases resembling tuberculosis. In most of the cases the symptoms were less severe than would be expected in view of the degree of pathological change, and consisted in moderate cough with scanty expectoration, fever, if any, of low type, and leucocyte count varying from normal to seldom more than 10,000 per cmm. The fungi from all cases appeared to be the same, except that 12 were pathogenic for laboratory animals, while the other 6 were not. Five of the cases are described in detail.

P. T.

TALICE (R. V.) & MACKINNON (J. E.). *Penicillium bertai* n. sp., agent d'une mycose broncho-pulmonaire de l'homme. [*Penicillium bertai* **n. sp., causing Broncho-Pulmonary Mycosis in Man.**]—*Ann. Parasit. Humaine et Comparée.* 1929. Mar. 1. Vol. 7. No. 2. pp. 97–106. With 1 text fig. [12 refs.] [Parasit Lab., Faculty of Med., Paris.]

Cultures of a fungus were obtained on three different occasions from the sputum of a case of pseudo-tuberculosis, in which acid-fast bacilli could not be detected directly or by guineapig inoculation. The fungus is considered to be a new species of *Penicillium* belonging to the sub-genus *Aspergilloides* and is named *Penicillium bertai*. Inoculation of a guineapig and a rabbit with the sputum, and intravenous inoculation of a rabbit with a spore suspension, gave negative results.

P. T.

CASTELLANI (Aldo). **Certain Bronchomycoses which may simulate Pulmonary Tuberculosis.**—*Jl. Trop. Med. & Hyg.* 1929. Jan. 1 & 15. Vol. 32. Nos. 1 & 2. pp. 1–8; 17–22. With 14 text figs. [2 refs.]

These papers contain a general account of various fungous diseases which may simulate pulmonary tuberculosis, together with descriptions of illustrative cases.

P. T.

PERUCHENA (José G.). Sobre un caso de moniliasis pulmonar. [**A Case of Pulmonary Moniliasis.**]—*Semana Méd.* 1929. Feb. 28. Vol. 36. No. 9 (1833). pp. 527–535. With 12 text figs. [20 refs.]

A man of 45 years complaining of cough, worse at night, fatigue and sweating. There were scattered râles over the right side; the temperature was normal. Radioscopy showed an infiltration of practically the whole of the upper lobe of the right lung. Tubercle bacilli were not found, but a Monilia was cultivated which differed from the known species in fermenting

laevulose and maltose only with gas production, slightly acidifying galactose and arabinose, and producing slight acid in milk without clot. The name proposed for it is *Monilia platensis*. The patient rapidly recovered after administration of potassium idoide, and the physical signs completely disappeared in a month.

H. Harold Scott.

RIBEIRO DA FONSECA (Olimpio Oliveira). Ensayo de revisión de las blastomicosis sud-americanas. [**Review of the South American Blastomycoses.**]—*Prensa Méd. Argentina.* 1928. Sept. 30. Vol. 15. No. 12. pp. 513–536. With 19 figs. [Oswaldo Cruz Inst., Rio de Janeiro.]

Diseases due to fungi are commonly regarded as among the most difficult in human pathology, and of these some of the most obscure are those denominated "blastomycoses." With a view to throwing light on these dark places the author describes the four chief blastomycoses met with in S. America. They are: (1) Granuloma coccidioides, Posadas-Wernicke disease, caused by *Coccidioides immitis*; (2) American blastomycosis proper, Gilchrist's disease, produced by *Mycoderma dermatitidis*; (3) Rhinosporidium, discovered by MALBRÁN, caused by *Rhinosporidium seeberi*; (4) Mazza and Parodi's mycosis associated with *Pseudococcidioides mazzai*. In the case of the first two the author gives an account of the history of the affection, the morphology and cultural characteristics of the parasites, the virulence in experimental animals, and the symptoms, pathology and treatment of the disease they produce in man. Remarks on the third are limited to an account of the history, the morphology and mode of growth. Of the fourth one case only has been recorded, that of an Argentine with a prelaryngeal abscess which opened and left a fistula, believed to be tuberculous until cultural examination showed the presence of a fungus which resembled *Coccidioides immitis*. Further investigation showed that it probably belonged to the Family Phycomycetoaceae, occupying a position between the Phycomycetes and the Ascomycetes. It is believed to be a new genus which, on account of its resemblance to *C. immitis*, has been named *Pseudococcidioides mazzai*, after MAZZA, who, with PARODI, observed this unique case in 1927.

H. Harold Scott.

BONNE (C.). Over blastomycosen, met beschrijving van een geval van chromoblastomycosis uit Sumatra. [**On Blastomycosis, with Description of a Case of Chromoblastomycosis from Sumatra.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1928. Vol. 68. No. 5. pp. 705–710. With 6 figs. on 3 plates. [8 refs.]

The name blastomycetes has lost its systematic significance from a botanic point of view. It is used for micro-organisms which, as seen in the tissues, show some resemblance to yeast cells, but which belong to various groups, as can be shown by their cultivation on appropriate media.

Bonne quotes ROCHA LIMA's classification of the blastomycetes in six groups (*Verhandl. der Deutschen Pathol. Gesellschaft*, 20e Tagung, 342, 1925) and gives a description of a case of chromoblastomycosis in a Batak male from Sumatra, who had suffered for about 7 years from this affection. The illustrations give a good idea of the case.

As far as appears from the literature on this subject blastomycosis is rare in the Dutch East Indies, and no case of chromoblastomycosis has been published.

W. J. Bais.

SMITH (D. C.), TURNER (H. C.) & SANDERSON (E. S.). **Systemic Blastomycosis, with Report of a Fatal Case.**—*Brit. Jl. Dermat. & Syph.* 1928. Aug.–Sept. Vol. 40. Nos .8–9. pp. 344–359. With 7 figs. on 3 plates. [12 refs.] [School of Med., Univ. of Virginia, Charlottesville.]

A case of blastomycosis in a man aged 42, a native of Virginia, terminated fatally after a duration of 7 months. The initial lesion occurred as a small nodule on the bridge of the nose, which attained the size of a pea and then ruptured and discharged bloody purulent matter. Later similar but larger nodules were developed all over the body, and the condition of the patient progressively became worse. At autopsy, in addition to numerous sub-cutaneous abscesses, lesions were found in the lungs, but other organs were not infected. Numerous yeast-like cells were present in pus from the lesions and in sections of the cutaneous and pulmonary lesions; and cultures of a blastomyces were readily grown from the pus. The fungus resembled those previously described from most cases of blastomycosis. Neither pus from the lesions nor cultures of the fungus were pathogenic for rabbits, guineapigs or mice.

P. T.

SILVA (Flaviano). Blastomycose generalizada. [**Generalized Blastomycosis.**]—*Brasil-Medico.* 1928. Oct. 6. Vol. 42. No. 40. pp. 1108–1112. With 3 text figs.

The patient was a man of 39 years, complaining of a sore which had started in the mouth four months before he came under the author's observation. By this time it had spread in the form of an ulcer with fungating edges involving both lips and the gums. Soon the cervical glands became enlarged and later other glands, and in spite of treatment, at first with large doses of potassium iodide (up to 12 gm. in the day) and afterwards with other drugs, the disease progressed and there was marked emaciation preceding death which occurred six months after he was first seen. Foci were found in the liver and the spleen, and microscopically were tuberculoid but without any caseation. *Coccidioides immitis* was cultivated from the lesions. The source was not discovered with certainty, but the patient confessed to picking up vegetables in the fields and eating them raw. He was also syphilitic.

H. Harold Scott.

PEÑA CHAVARRIA (A.). La blastomicosis de las mucosas naso-buco-faringea, según observaciones hechas en varios países de la América Latina. [**Blastomycosis of the Mouth and Naso-pharynx in Latin America.**]—*Crónica Méd.* Lima. 1928. July. Vol. 45. No. 781. pp. 210–216.

The condition herein described is probably more common than is believed, owing to its resemblance to leishmaniasis and destructive syphilitic lesions, and the consequent diagnosis being made of one of the latter. Its resemblance clinically to the former is fairly close, but the microscope clears up the difficulty except when the two co-exist. The lesion starts as a small ulcer which spreads rapidly, destroying

soft tissues, then cartilage, and rarely even bone, so that perforation of the palate, ulceration and destruction of the nose, pharynx and larynx produce a most unsightly condition.

In some cases, while destruction is progressing at one part, hypertrophy resembling rhinoscleroma, for example, may be seen at another.

H. Harold Scott.

DE ALMEIDA (Floriano Paulo). Aspectos histologicos dos casos de blastomycose verificados em S. Paulo. [**Histology of Blastomycosis as met with in S. Paulo.**]—*Brasil-Medico.* 1929. May 4. Vol. 43. No. 18. pp. 485–489. With 21 figs.

The author has met with 160 cases of blastomycotic infection in various states of Brazil; 90 per cent. of them occurred in S. Paulo. He has studied histologically 60 of them and describes the appearance of the fungus when stained by the Goodpasture-MacCallum or Gram-MacCallum method. In many the parasite showed as a single darkly staining spherical mass which might be made up of closely aggregated minute granules; in others the internal structure was looser and the periphery was bounded by a circle of granules. Occasionally the individual bodies were smaller and disposed either in pairs or rarely in chains of five or six elements. [The tissue reactions to the presence of the parasite are not described and unfortunately the microphotographs are too faintly reproduced to be of much value in this respect].

H. Harold Scott.

SPRING (Dorothy). **Comparison of Seven Strains of Organisms causing Blastomycosis in Man.**—*Jl. Infect. Dis.* 1929. Mar. Vol. 44. No. 3. pp. 169–185. With 5 text figs. [11 refs.] [School of Med., Univ. of Pennsylvania, Philadephia.]

Seven strains of fungi isolated from cases of American blastomycosis of Gilchrist were compared as regards cultural characters; growth in hanging-drop; fermentation tests; resistance to dyes and heat; and pathogenicity to animals. The various strains were found to differ markedly in all these respects. Animal inoculations showed that chickens are not susceptible to subcutaneous inoculation; rabbits are only slightly susceptible even to intravenous inoculation; guineapigs are comparatively resistant; white rats are comparatively susceptible to infection although it is not fatal to them; and white mice are the most susceptible of the animals tested and are the only ones in which generalization of the disease occurred.

P. T.

HOFFMANN (W. H.). La cromoblastomicosis en Cuba y la enfermedad de Guiteras o "Chappa." [**Chromoblastomycosis in Cuba and Guiteras's Disease, "Chappa."**]—*Rev. Méd. Cubana.* 1928. Apr. Vol. 39. No. 4. p. 420.

Professor Hoffmann states that the various affections included under the term "blastomycosis," namely the European form of Buschke and Busse, produced by Saccharomycetes, the American form, Gilchrist's disease, due to a Cryptococcus, Escomel's South American form, confused with leishmaniasis, and Fonseca's Brazilian form, Granuloma

coccidioides, should really be denominated Ascomycetes. The causative fungus is believed to live saprophytically on the skin, but when it gains entrance through an abrasion or other wound it assumes pathogenic properties and may lead to extensive ulceration. The affection described by READ in 1901 under the name "chappa" and of which ten cases have been studied by GUITERAS, is considered one of the same group. It starts as a small circumscribed focus in the skin, at the site of a superficial lesion, and by extension an ulcer results which involves even bones and joints and produces great deformity, although the general state remains unaffected unless secondary infection supervenes.

H. Harold Scott.

JACOBSON (H. P.). **Coccidioidal Granuloma.**—*California & Western Med.* 1928. Dec. Vol. 29. No. 6. pp. 392–396. [1 ref.] [General Hosp., Los Angeles.]

Four cases of Coccidioidal granuloma are described, in all of which treatment with colloidal copper was given. One case terminated fatally; but in the other three cases the treatment resulted in great improvement, and possibly in cure.

P. T.

TOMLINSON (C. C.) & BANCROFT (Paul). **Granuloma Coccidioides. Report of a Case responding favourably to Antimony and Potassium Tartrate.**—*Jl. Amer. Med. Assoc.* 1928. Sept. 29. Vol. 91. No. 13. pp. 947–950. With 6 text figs. [11 refs.] [College of Med., Univ. of Nebraska, Omaha.]

This case of Granuloma coccidiodes, which occurred in a man aged 26, appears to have arisen as a laboratory infection through working with cultures of *Coccidiodes immitis* [*Mycoderma immite*]. For a period of three months intravenous injections were given of 1 per cent. antimony and potassium tartrate on alternate days, in doses varying from 2 to 8 cc. During the same period half a skin unit of unfiltered X-ray was given at intervals of 10 to 14 days. This treatment apparently resulted in a complete cure, and the patient has been in excellent health and free from all symptoms for twelve months.

P. T.

i. REIMANN (Hobart A.), KUROTCHKIN (Timothy G.) & TSO (Edith). **Studies on the Etiology of Splenomegaly of Unknown Origin. (Splenic Mycosis?)**—*Proc. Soc. Experim. Biol. & Med.* 1929. Mar. Vol. 26. No. 6. pp. 410–413. With 2 text figs. [9 refs.]

ii. HU (C. H.), REIMANN (Hobart A.) & KUROTCHKIN (Timothy G.). **Filaments in Siderotic Nodules of Spleen in Cases of Splenomegaly of Unknown Origin.**—*Ibid.* pp. 413–416. With 3 text figs. [9 refs.] [Peking Union Med. College, Peking, China.]

i. Spleens and portions of liver were examined from 3 cases of splenomegaly and one of cirrhosis of the liver occurring in Northern China. Inoculation of crushed splenic pulp on Sabouraud's medium gave cultures of fungi in each case; but no growth was obtained in tubes inoculated with liver. The fungus from one case resembled a Penicillium and proved to be pathogenic for rabbits, guineapigs and mice. The fungus from the other 3 spleens is as yet unclassified and was not pathogenic for laboratory animals.

ii. The authors found that by appropriate staining methods the mycelial-like filaments present in siderotic nodules from cases of splenomegaly may be seen to be continuous with normal tissue fibres. They also found that the staining reactions and morphology of these filaments are different from those of fungi isolated from the same spleens. Hence they conclude that the filaments in the nodules are not fungous hyphae.

P. T.

DA FONSECA (Olympio) & LEAO (A. E. de Arêa). [In Portuguese & English.] A questão das esplenomegalias mycosicas. **The Question of Mycotic Splenomegaly.**—*Inst. Oswaldo Cruz, Supplemento das Memorias.* 1928. Aug. 31. No. 1. In Portuguese pp. 10–15. With 2 text figs. & 3 figs. on 2 plates. In English pp. 16–22. [24 refs.] [Oswaldo Cruz Inst., Rio de Janeiro.]

The recent discussion as to the mycotic origin of splenomegaly led the authors to reinvestigate the material from cases of splenomegaly in the Oswaldo Cruz Institute. Some cases showed ill-defined Gandy-Gamna nodules; but in others the nodules were well-defined, and stained sections showed various structures superficially resembling mycelial elements. In no case, however, were undoubted fungus hyphae seen, and the authors agree with GAMNA and LANGERON that such structures are really formed by degeneration of the diseased tissues.

P. T.

JAFFÉ (R. H.) & HILL (L. R.). **Splenic Mycosis.**—*Arch. Pathology.* 1928. Aug. Vol. 6. No. 2. pp. 196–209. With 5 text figs. [18 refs.] [Dept of Path., Univ. of Illinois & Uihlein Memorial Lab., Grant Hosp., Chicago.]

Siderotic nodules resembling those described by NANTA, WEIL and others, were found in spleens from two cases of juvenile splenomegalic anaemia, three cases of sickle-cell anaemia and one case of tuberculosis of the spleen. Structures believed to be fungous hyphae and fructifications were present in the nodules; and from one case of juvenile splenomegalic anaemia cultures of a fungus resembling *Aspergillus fumigatus* were obtained. The authors consider that the anaemia is not caused by the fungus, and favour the view that pathological changes in the spleen predispose it to invasion by various aspergilli.

P. T.

NANTA (A.). Splénomégalie aspergillaire expérimentale et splénite mycosique spontanée de l'animal. [**Experimental Aspergillary Splenomegaly, and Spontaneous Mycotic Splenitis of Animals.**]—*C.R. Soc. Biol.* 1928. Dec. 14. Vol. 99. No. 36. pp. 1785–1787. [2 refs.]

Cases of spontaneous splenitis of the pig appear to be due to an Actinomyces. The author suggests that cases may be due to actinomycotic forms of Aspergilli, such as were obtained experimentally by LUCET and others with *Aspergillus fumigatus* and *Sterigmatocystis nidulans.* He has described actinomycotic forms of *S. nantae* following experimental inoculation of animals, and he considers that these forms may be important in relation to splenomegaly in man, which he and others believe to be of mycotic origin.

P. T.

CLEMENTE (Giuseppe). Sulla micosi sperimentale della milza. [**Experimental Mycosis of the Spleen.**]—*Pathologica.* 1928. July 15. Vol. 20. No. 441. pp. 335–343. With 9 figs. on 2 plates. [16 refs.] [Inst. Clin. Chirurg., Univ., Palermo.]

In a certain number of cases of splenomegaly organisms of a streptothrix (GIBSON) or mycotic nature (NANTA, PINOY) have been found on histological examination and have received various names—*Aspergillus* or *Sterigmatocystis nidulans*, *A. nantae*, etc.—but the only sure conclusion has been that it is an Aspergillus but not *A. fumigatus*. The malady has been regarded as a new disease of the spleen, part of the large group " splenomegaly." Thus, OBERLING has studied 200 cases of splenomegaly and has reported lesions of " Nanta's mycosis " in four cases of Banti's disease, two of haemolytic jaundice, several of cirrhosis of the liver, a lymphocytic leukaemia and an infarct of spleen in a subject with arteriosclerosis.

Two questions arise: (1) Is the lesion a mycotic one at all? (2) If it is, is the disease due primarily to the mould, or is this a secondary invader of an organ already affected from some other cause?. GAMNA, ZORINI, and LANGERON, among others, deny the mycotic element and consider the filaments to be the result of regressive changes in collagen fibrils, or of necrosis and disintegration of elastic and connective tissue elements. The important fact remains that up to the present the lesions found have not been reproduced experimentally in animals.

The author inoculated into the spleen of guineapigs, rabbits, rats and dogs, emulsions of spores of a ten-day culture of *A. fumigatus*. Certain lesions resulted which are described in the text and illustrated by microphotographs, and these corresponded closely with those found by NANTA.

[The above abstract has been given because a subject so important as this should be widely known in order that more intensive work may be undertaken to solve the problem, but in the opinion of the reviewer the author's experiments are beside the mark; they merely prove that injection of spores of *A. fumigatus* into the spleen will produce certain results there, and leave untouched the main question as to whether what was seen by NANTA and PINOY are moulds and if so, whether they are pathogenic.]

H. Harold Scott.

PETZETAKIS (M.) & PAPADOPOULO (J.). Formes filtrables dans les cultures d'un champignon isolé d'un cas de splénomégalie égyptienne et intradermoréaction mycosique. [**Filterable Forms in Cultures of a Fungus isolated from a case of Egyptian Splenomegaly and Mycotic Intradermal Reaction.**]—*C. R. Soc. Biol.* 1928. June 29. Vol. 99. No. 22. pp. 274–275. [1 ref.]

Cultures on ordinary broth of a fungus isolated from a case of Egyptian splenomegaly were incubated for 7 days and filtered through an L candle. No micro-organisms were detected in the filtrate by direct examination, staining or after centrifugation; and inoculation of the filtrate on Sabouraud's agar was negative. On incubation, the filtrate showed cloudiness on the 4th day and rare coccus-like organisms were present. Bacillary forms appeared on the 5th day and in from 7–10 days mycelium developed, which resembled that of ordinary

cultures of the fungus. After 4 days' incubation, the filtrate gave rise to cultures of a similar mycelium when inoculated on Sabouraud's medium.

Intradermal injection of 1 cc. of the filtrate into a subject with splenomegaly caused no reaction; but similar injection of 0·25 cc. of the filtrate into a normal subject resulted in an intense reaction lasting 48 hours.

P. T.

FAWCETT (John) & GIBSON (A. G.). **A Case of Splenic Anaemia due to a Streptothrix Organism.**—*Lancet.* 1928. June 9. pp. 1171–1173. [6 refs.]

A Streptothrix was cultivated on serum broth from the Gandy-Gamna nodules present in the spleen removed from a case of splenic anaemia. Three intraperitoneal injections of cultures emulsified in saline proved pathogenic for a monkey (*Macacus sinicus*). The symptoms were gradual decline in health, enlargement of the spleen, persistance of appetite and tenderness of the abdomen; with a terminal infection with the tubercle bacillus. The streptothrix was recultivated from the blood.

P. T.

LUSENA (Marcello). Splenomegalie con micosi. [**Splenomegaly with Mycosis.**]—*Riforma Med.* 1928. Nov. 26. Vol. 44. No. 48. pp. 1549–1560. With 3 coloured figs. on 1 plate & 1 text fig. [Refs. in footnotes.] [Inst. of General Clin. Med., Univ., Padua.]

This form of enlargement of the spleen, which is not found to have any association with the usual conditions of splenomegaly, is now being given the name of Primary thrombophlebitic splenomegaly. GAMNA himself named it Splenogranuloma sideroticum. Two cases are recorded with a well-reproduced coloured plate showing the histological changes in the spleen. The distinctive feature is the presence of Gandy-Gamna nodules. The important components of these are perivascular infiltrations, with aggregation of red corpuscles, fragments of hyphae believed to be Aspergillus, and multinucleated giant-cells some of which also contain hyphal fragments. The nodules seem to be definitely related in position to the vessels. The name "sideroticum" was given because of the presence of iron in the nodules. Nothing is known as to the aetiology.

H. Harold Scott.

PEEL (Albert A. F.). **The Cultivation of an Organism from the Spleen in a Case of Banti's Disease.**—*Jl. Path. & Bact.* 1928. July. Vol. 31. No. 3. pp. 591–593. [2 refs.] [Eastern District Hosp., Glasgow.]

Cultures of an Actinomyces-like organism were obtained on blood agar from the extirpated spleen in a case of Banti's disease.

DE VECCHI (Bindo). Considerazioni istogenetiche sui cosidetti "noduli di Gamna." [**Gandy-Gamna Nodules.**]—*Haematologica.* Pavia. 1928. Vol. 9. No. 5. pp. 459–499. With 3 coloured figs. on 1 plate. [34 refs.] French Summary p. 499. [Inst. Anat. Path., Univ., Florence.]

Under this name are described certain small nodular deposits in the spleen. Their nature is not known. Several suggestions have been made, the chief being that they are mycotic and due to *Aspergillus* (*Sterigmatocystis*) *nidulans*. This, however, is quite unproved, the histology of the

lesions being that of a granuloma, the foci of which coalesce and in which pigment is either deposited or produced locally. In many cases they appear to be localized calcifications in the walls of the splenic vessels.

H. Harold Scott.

PETZETAKIS & PAPADOPOULO (J.). Premier cas de mycétome de la rate observé en Egypte sur un champignon isolé en culture pure après ponction de la rate dans un cas de splénomégalie égyptienne. [**Egyptian Splenomegaly due to a Fungus Isolated in Pure Culture.**]—*Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1928. July 26. Year 44. 3rd Ser. Vol. 52. No. 26. pp. 1292–1294.

This paper is the same as one previously published by the same authors [See this *Bulletin*, 1928, Vol 25. p. 751.]

P. T.

CASTELLANI (Aldo). **Blastomycosis and Some Other Conditions due to Yeast-Like Fungi (Budding Fungi.)**—*Amer. Jl. Trop. Med.* 1928. Sept. Vol. 8. No. 5. pp. 379–422. With 20 figs. [13 refs.] [Dept. Trop. Med., Tulane Univ. of Louisiana, New Orleans.]

This paper, except for rearrangement, is essentially the same as one already published elsewhere. [See this *Bulletin*, 1928, Vol. 25, p. 742.]

P. T.

GALBREATH (W. R.) & WEISS (Charles). **Bronchomoniliasis. Report of a Case from Porto Rico.**—*Arch. Intern. Med.* 1928. Oct. Vol. 42. No. 4. pp. 500–507. [8 refs.] [Presbyterian Hosp., & School of Trop. Med., Univ. of Porto Rico, San Juan.]

This report was previously published in *Porto Rico Rev. of Public Health and Trop. Med.* 1928. March. [See this *Bulletin*, 1928, Vol. 25. p. 747.]

P. T.

MONTPELLIER (J.), CATANEI (A.) & CATTOIR. Sur un nodule dermique dû à une épine végétale souillée par un champignon. [**A Dermal Nodule due to a Thorn infected with a Fungus.**]—*C.R. Soc. Biol.* 1929. Feb. 15. Vol. 100. No. 6. pp. 408–410.

Cultures of an Alternaria were obtained from a thorn extracted from within a dermal nodule of 7 months' duration.

P. T.

CASTELLANI (Aldo). I miceti e la medicina tropicale. Conferenza tenuta il 30 settembre 1928, in Torino, al I Congresso Italiano di Medicina ed Igiene Coloniale.—*Riforma Med.* 1928. Oct. 22. Vol. 44. No. 43. pp. 1377–1380; 1383. With 3 text figs.

MEDICAL ZOOLOGY.

i. FAIRLEY (N. Hamilton). **The Present Position of Snake Bite and the Snake Bitten in Australia.**—*Med. Jl. Australia.* 1929. Mar. 9. 16th Year. Vol. 1. No. 10. pp. 296–313. With 5 text figs., 2 graphs & 23 figs. on 6 plates (1 coloured). [34 refs.]

ii. ——. **The Dentition and Biting Mechanism of Australian Snakes.**—*Ibid.* pp. 313–327. With 14 figs. [10 refs.] [Walter and Eliza Hall Inst. of Research, Melbourne.]

i. Very timely has the author been stirred to revive a brilliant chapter in the Australian annals of science, and it is with gratitude that one must notice his judicious confirmations and amplifications of it.

From his study of the records and from his own work he concludes that of the many venomous Australian land-snakes (the sea-snakes are not here included) the really deadly ones are, in dismal precedence, the Death Adder (*Acanthophis antarcticus*), the Tiger Snake (*Notechis scutatus*), the Copperhead (*Denisonia superba*), the Brown Snake (*Diemenia textilis*), and the Black Snake (*Pseudechis porphyriacus*). In respect of the quality of their lethal power (as tested by subcutaneous injection of solutions of minimum lethal doses of their dry venom into sheep of 88 lb.) that of the Death Adder is 10 times, that of the Tiger Snake is 25 times, that of the Copperhead 2½ times, and that of the Black Snake is one-third, that of the Indian cobra. In respect of the volume of their lethal power (as estimated by the number of mortal doses contained in the *average* discharge of their venom-glands, as delivered at a single " milking " of the snake) that of the Death Adder would kill 84, that of the Tiger Snake would kill 118, that of the Copperhead would kill 8·9, and that of the Black Snake would kill 1·5 sheep of 88 lb. [These are the numbers of mortal doses contained in the *average* of yields (far below the maximum yield obtained), and they are based on " milkings " of snakes in captivity—and captivity is known to be often inhibitory of the secretion of venom.]

The author duly emphasizes the very important point that the mortal issues of snakebite depend not only on virulence of venom but hang equally on the efficiency of the mechanism (of fang, jaw, etc.) by which it is injected. When, as in the Death Adder, the fangs are larger and the maxillae that carry them are shorter and more readily erectile, then the strike will be surer and go deeper and more venom will get home, and it is in this consideration that the Death Adder—which also has a larger command of venom—is here branded as the most dangerous of all Australian snakes. At the other extreme is the Brown Snake with short fangs, long and little-mobile maxillae, and the smallest and least prolific venom-glands.

The physiological effects of the five venoms are fully discussed in the combined light of the older observers' and the author's own experiments. Like all colubrid venoms they all are powerfully neurotoxic, and it is the neurotoxin that the author calls their " killing constituent " —death being brought by paralysis of respiration. The author does not mention the Brown Snake, but all the other four are also haemolytic and haemorrhagic, and in sheep multiple haemorrhages can almost invariably be demonstrated after death, particularly in the lungs and in the subperitoneal tissue at the base of the mesentery ; but extensive

extravasation in the vicinity of the bite is rare. The venoms of the Tiger Snake (*Notechis scutatus*) and the Black Snake (*Pseudechis porphyriacus*) exercise furthermore an initial thrombotic power. Sheep that received only one lethal dose of the Notechis venom generally died in 1 to 4 hours, from thrombosis of the portal vein and its tributaries, and the splenic vein might clot and the spleen be swelled to more than five times its normal weight. Larger doses were fatal in 20 minutes or less, and then clots in the right heart were generally found. The venom of the Copperhead (*Denisonia superba*) contains an anticoagulin, in addition to the toxins first mentioned, but no thrombase.

On the practical side the clinical aspects and the treatment of snake-bite are described and discussed. The local lesions are slight, as in Colubrids generally. Due, but very necessary, emphasis is placed upon the fact that the time and onset of the systemic manifestations depend upon the amount of venom injected. The fundamental principles of treatment are clearly explained, with due insistance on the awful rapidity of absorption of venom. In respect of ligature it is admitted that even against these horribly lethal snakes it would have *some* utility in prolonging the precious time available for treatment *if* it could be applied *immediately*, as under experimental conditions. In several experiments when 55 to 70 certain lethal doses of Tiger Snake venom were injected into the already ligatured leg of a sheep no symptoms followed so long as the ligature remained affixed (4 to 6 hours), though death ensued 2 to $2\frac{1}{2}$ hours after its removal. Again, in another experiment, four sheep with forelegs shaved were allowed to be bitten in the foot by a Tiger Snake of average size; (the snakes used were seen to bite effectively, and residual venom could be "milked" from them afterwards); then an effective rubber tourniquet was affixed at the level of the upper part of the cannon bone, this being done *immediately* to three of the sheep, and about two minutes after the bite to the fourth; thereafter about $2{\cdot}9 \times 2{\cdot}9$ cm. of skin and subcutaneous tissue, bite included, were cut away, the wound was dressed with strong solution of $KMnO_4$, and the ligature left for 30, or 45, or 165 minutes. The one sheep that had not been ligatured *immediately* died 3 hours and 25 minutes after being bitten; the other three showed no symptoms. This is the best that the author can find to say for immediate ligature, *combined with excision*, as a means of saving life after a really effective bite and the injection of a formidable charge of venom; and this seems to have been hitherto the usual method of treating snake-bite in Australia. But now antivenenes for the two most deadly Australian snakes—the Tiger Snake and the Death Adder—are in process of manufacture.

From the local records of 281 cases the author finds that 56 per cent. were bites on the leg—all but 5 of the bites below the knee; and 42 per cent. were bites on the arm—only 8 bites above the elbow. It is pointed out that most of those below the knee could have been prevented by boots and leggings or putties; since a snap bite by a Tiger Snake on a sheep whose leg was clad in a thick woollen stocking proved fatal in an hour and 25 minutes, but when a woollen stocking was covered by two layers of army regulation putti natural bites by both Tiger Snake and Death Adder were ineffective, since the venom only got as far as the sock.

This bare abstract concentrates chiefly on the author's original work, which is so critically combined with previous knowledge as to give the paper a very broadly educational value.

ii. This is a fine anatomical study, full of descriptive detail and discerning comment, and liberally illustrated, of the venom apparatus of the Proteroglyph colubrines, with special reference to the five deadly Australian species above named and to practical application in the diagnosis and prognosis of their bite. It includes the venom-glands, the suspensorium of the jaws, the bones and muscles that give mobility to the palate and maxilla, the dentition, the poison-fangs and their scope of movement as studied in moulds and models, and by electrical stimulation of appropriate muscles in the living snake deprived of brain—in short all that rather intricate mechanism that give formidable accuracy to the injection of the venom. Its result shows that the Death Adder (*Acanthophis antarcticus*) has the most effective injecting apparatus, and the Brown Snake (*Diemenia textilis*) the least effective, with, in that order intermediate, the Tiger Snake (*Notechis scutatus*), the Black Snake (*Pseudechis porphyriacus*), and the Copperhead (*Denisonia superba*).

The more dangerous efficiency of the Death Adder is due to the facts that while its maxilla is the shortest in proportion to the skull (length of skull 3·72 times that of maxilla) and has its dentition reduced to 1 or 2 small teeth besides the very large functional fang, its quadrate bone is the longest in proportion to the skull (length of skull twice that of quadrate bone), this being a correlation of parts that confers a greater degree of mobility on the maxilla and consequently of elevation to the fangs in the act of biting (elevation of fangs=40° to 50°). Indeed, in mobility of palate and maxilla, erectile power of fang, and proportional length of quadrate bone the Death Adder shows a suggestive approximation to the Viperids, as the author observes ; furthermore the Death Adder has a broad viperoid snout, which implies a broader space between the fangs and a wider distribution of venom, and this broader interspace is one among the characteristic impressions left in a mould of its bite.

In the Tiger Snake the length of the skull is 3·56 times that of the maxilla and 2½ times the length of the quadrate bone, the possible elevation of the fangs is 30°–35°, and the average number of teeth behind the fang is 3. In the Copperhead the length of skull is 3·4 times that of maxilla and 3·1 times that of quadrate, the possible elevation of the fangs is 25° 30°, and the number of teeth behind fang 4·5. In the Black Snake the length of the skull is 3·28 times that of maxilla, and 2·9 times that of quadrate, the possible elevation of fangs 25°–30°, and the number of teeth behind fang 4. In the Brown Snake the length of the skull is 2·65 times that of maxilla and 3·45 times that of quadrate, the possible elevation of fangs is 10°–15°, and there are 7·25 teeth behind the fang. The osteological facts, which, as the author remarks, show a graduated harmony from the Colubrine aglyph type to the Viperid type are extremely interesting, although the author is mistaken in supposing that his method of eliciting and stating them has in it anything novel to zoologists. [What zoologists will appreciate is not another instance of a familiar and fundamental method, but the evidence supplied by Fairley that this Crotaline-like Acanthophis seems to be a link between the Crotaline viperids and the Elapine colubrids, and the support that the existence of this remarkable snake in Australia gives to the well-known theory of a former land or shallow-sea and island-chain connexion (in Miocene times) between Australasia and South America—wealth in Crotaline snakes being one of the characteristic features of the American fauna.]

A. Alcock.

MEDICAL JOURNAL OF AUSTRALIA. 1929. Mar. 16 & 23. 16th Year. Vol. 1. Nos. 11 & 12. pp. 336–365; 372–394.—**Symposium on Snake Bite.** [Walter & Eliza Hall Inst. of Research, Melbourne.]

I. **Venom Yields in Australian Poisonous Snakes.** [FAIRLEY (N. Hamilton) & SPLATT (Beryl).] pp. 336–348. With 1 graph. [7 refs.]

I. In the introduction to this instructive paper the authors explain that accurate knowledge of the amount of venom that may be discharged by a given species of poisonous snake is necessary both for estimating the potential danger of its bite and for determining the quantity of antidote (antivenom) that may be required for the treatment. But when a snake bites it seldom discharges the whole contents of its venom glands, so that for greater accuracy, as well as for settling the practical question how far a snake continues dangerous after it has inflicted a first bite, it is necessary also to know how much (if any) venom (reserve venom) can be squeezed ("milked") from the venom glands immediately afterwards. In the statistics of their work the authors use the term "total venom" as including both the venom discharged at biting and the reserve venom, and the term "primary yield" to mean the total venom that can be obtained from a fresh captured snake.

The introductory remarks also include an account of the habits, habitats, and local distribution of the Australian venomous snakes, critical notes on the care and feeding of snakes in captivity, comments on the parasites and diseases of snakes, and a full and critical account of methods of collecting and preserving venom.

The five Australian snakes here considered are (1) the Tiger Snake (*Notechis scutatus*), (2) the Death Adder (*Acanthophis antarcticus*), (3) the Copperhead (*Denisonia superba*), (4) the Black Snake (*Pseudechis porphyriacus*), and (5) the Brown Snake (*Diemenia textilis*). Of No. 1 the average primary yield of 20 healthy snakes was 34·9 mgm. of dried venom, and the highest individual yield 155 mgm. Of No. 2 the average primary yield of 41 mature snakes was 78·2 mgm., and the highest individual yield 235·6 mgm. Of No. 3 the average primary yield of 56 snakes was 40·1 mgm., and the highest individual yield 189·6 mgm. Of No. 4 the average primary yield of 6 snakes was 37 mgm., and the highest individual yield 74·8 mgm. From No. 5, although 7 specimens were milked no venom was obtained; but TIDSWELL's thirteen observations are cited, who found the average yield of its dried venom to be 4·8 mgm., with a highest yield of 5·56 mgm.

The individual yields of venom in all the species vary very much; large heavy snakes naturally give the highest yields, and the authors emphasize the observation that individuals that have the fangs widest set apart can inject the most venom. Again, besides various circumstances in the natural or artificial environment that may affect the individual snake adversely, the authors mention two pathogenous snake-parasites—a lung-fluke (*Dolichopera maculpini*) and a larval tapeworm (Sparganum)—that may exercise a check on secretion of venom.

The statistics justify the authors' conclusion that the Australian thanatophidia must be regarded as still very dangerous after they have bitten a victim—by reason of their large amount of reserve venom. For instance, in 75 observations of Death Adders in which the average

" total yield " of venom was 79·1 mgm. the amount of reserve venom obtained by milking, after biting, was 21·6 mgm. ; and in 35 observations of Tiger Snakes the corresponding figures were 43·5 mgm., and 14·1 mgm.

II. **The Venom of** *Notechis scutatus.* [KELLAWAY (C. H.).] pp. 348–358. With 3 graphs. [7 refs.]

II. This is a study of the effects, as shown both in life and after death, of the venom of the Tiger Snake (*Notechis scutatus*) after subcutaneous injection of definite lethal doses into various species of mammals—horse, cat, monkey, rabbit, guineapig, rat, and mouse. Its conclusions are that for all these species death is due to the neurotoxic constituents of the venom and that the symptoms and the gross post-mortem findings have a general uniformity, but that the haemolytic and thrombotic effects of the venom show differency in the species. The heavier individuals of a species are more susceptible to the venom than the lighter individuals ; and quite independent of this, the lethal doses for the different species show that the average size and weight of the species also have something to do with the susceptibility of that species—for example, the minimum lethal subcutaneous dose for a horse is 0·005 and for a sheep 0·01 mgm. per kilogm. of body-weight, while that for a cat is about 0·10 and for a mouse more than 0·25 mgm. per kilogm. of body-weight. It seems probable that the lethal dose for man lies between that for the horse and that for the sheep. The incidence of blindness in animals recovering from sublethal doses of the venom is a noteworthy feature.

III. **A Preliminary Note on the Venom of the Australian Copper-Head** (*Denisonia superba*) *:* **its Toxic Effects in the Common Laboratory Animals.** [KELLAWAY (C. H.).] pp. 358–365. With 1 graph.

III. This is a preliminary study similar to the above (the animals of experiment being the cat, guineapig, rat, and mouse) of the venom of the Copperhead (*Denisonia superba*). This venom contains neurotoxin (the lethal component), haemorrhagin, and haemolysin, but not thrombase. The lethal dose for man is estimated as between 1·4 and 0·02 mgm. per kilogm. of body-weight.

IV. **A Preliminary Note on the Venom of** *Pseudechis guttatus* [KELLAWAY (C. H.).] pp. 372–377. [3 refs.]

IV. This is a preliminary account of limited experimentation with a small amount of venom from a single specimen of *Pseudechis guttatus.* The venom contains thrombase, haemolysin, haemorrhagin, and neurotoxin, but the haemolytic power is greater and the coagulant power less than that of other species studied. Thus, in the small animals used, haemorrhages in the lungs were usually observed and intense (frequently haemorrhagic) oedema spreading from the site of injection. " The pathological changes produced by subcutaneous injection . . . in small animals, particularly in the guineapig, resemble those produced by diphtheria toxin."

V. **Criteria for determining the Efficacy of Ligature, in Snake Bite. (The Subcutaneous-Intravenous Index.)** [FAIRLEY (N. Hamilton).] pp. 377–394. [14 refs.]

V. To appreciate its precision and well-reasoned completness this paper must be read in full. It is an investigation of the value of ligature in the treatment of bites from Australian venomous snakes, but its intelligence carries far beyond that goal. It begins with a historical review of the rational use of ligature, dwelling on WEIR-MITCHELL, who regarded it as a temporary respite and as giving time for other remedies, and preferred intermittent ligature because it could be maintained longer ; MARTIN, who thought it did more than this, and subsequently suggested its useful copartnery with a thermolabile fibrin ferment that fixed the venom locally ; ACTON & KNOWLES, who confirmed this local locking effect in the case of Russel's Viper venom rich in thrombase ; VITAL BRAZIL who regards it merely as prolonging time for employing other treatment, and CRIMMINS who thinks it thus far useful in giving time for applying mechanical suction.

Experimental work and methods are described at length. They included, for comparison, experiments with the venom of the Indian Cobra and the Russell's Viper, and they involved, as a preliminary, the determination of the " certainly lethal dose " (a dose just in excess of the ascertained minimum lethal dose) of each kind of venom for each species of animal used, not only subcutaneously but by the intravenous method, and the calculation of what the author calls the " subcutaneous-intravenous index." This index, which is expressed in milligrammes of venom per kilogram of body-weight of animal, is determined for each species of animal by dividing the subcutaneous by the intravenous certainly lethal dose. It appears that, in the absence of any considerable amount of haemorrhagin in a venom, subcutaneous injection will afford an index of the neurotoxic qualities and intravenous injection an index of the thrombase constituents of that venom, and hence that the subcutaneous-intravenous index can be employed to determine the relative susceptibility of a particular species of animal to those two " substances." Thus the author shows that with a typical Colubrid venom (Australian Death Adder and Copperhead) rich in neurotoxin and free from thrombase, there is not much difference between the subcutaneous and the intravenous mortal doses—though of course, death is slower by the former route—and the subcutaneous-intravenous index is therefore low. On the other hand, with a typical Viperid venom, rich in thrombase and poor in neurotoxin, the mortal intravenous dose is very much less than the mortal subcutaneous dose, and the index is high. But there may be Colubrid Venoms (Australian Notechis and Pseudechis) which contain much thrombase as well as much neurotoxin but not much haemorrhagin, and here too the index is low. Or, as with the venom of Russell's Viper, there may be much thrombase along with much haemorrhagin, and here the index is high. All that can be said therefore is that ligature is never successful where the subcutaneous-venous index of the venom is low.

In the experiments to test the value of ligature sheep were the standard animals used ; subcutaneous injections of certainly lethal doses of venom were made into the right forefoot ; and immediately after the injection the ligature was stretched so tightly round the cannon-bone as to ensure stasis, and was kept on for 30 to 35 minutes. Under these experimental conditions ligature did not appreciably lengthen the interval before death after injection of Tiger Snake (Notechis) venom,

although this venom is rich in thrombase, and although MARTIN had shown that ligature could protect rabbits from it and also from Pseudechis venom. (The explanation of this incongruity is that the rabbit is abnormally sensitive to thrombase, to which the sheep and goat are relatively insusceptible). Ligature was equally ineffective against the venom of the Death Adder (Acsanthophis), which does not contain thrombase. With venom of the Copperhead (Denisonia), which also is destitute of thrombase, one of a series of six ligatured sheep recovered after two days complete paralysis, and this recovery is thought to be due more likely to the natural resistance of the individual than to the ligature. Experiments on sheep under the same conditions with Indian Cobra venom confirmed the non-effectiveness of ligature except for slightly prolonging the interval before death ; no evidence of the action of thrombase was found after death, so that in this as in other respects the venom of the Indian cobra resembles that of the Death Adder and Copperhead. Comparison was also made with Russell's Viper venom as a standard viperine venom. Three out of five sheep recovered after reception of 1 to 1·2 certainly lethal doses, " and it is only reasonable to attribute this life-saving result to the effects of ligature "; but on the other hand three out of four that received less than the estimated lethal dose died despite ligature ; even in the fatal cases, however, some modification of the clinical and pathological course resulted and the interval preceding death was prolonged. This testimony to the life-saving possibility of ligature in cases of bite from Russell's Viper is in harmony with the observations of ACTON and KNOWLES.

Though these careful experiments on sheep discredit ligature as a therapeutic measure for the bites of Australian Elapines, they do not discountenance its value as a means of prolonging life and affording time for other treatment in all other countries.

A. A.

MEDICAL & SCIENTIFIC ARCHIVES OF THE ADELAIDE HOSPITAL. 1927. No. 7. pp. 18–20.—**Fatal Case of Tiger-Snake** (*Notechis scutatus*) **Bite.**

The victim was bitten in the left arm (only one puncture was observed subsequently) and, believing himself to be immune, he simply sucked the wound and applied a ligature to the arm ; but he very soon had nausea, headache, and pain in the axilla. Vomiting quickly followed, the vomit at last becoming dark-coloured. When admitted to hospital about 9 hours after being bitten, the victim was showing signs of paralysis—staggering, dysphradia, diplopia, ptosis—the circumference of the wound was ecchymosed and the whole arm was swollen, there was constant desire to defaecate and micturate and the urine contained blood. The bitten part was then excised and the wound treated with solid $KMnO_4$; later some sort of " African " antivenom was injected intravenis and stimulants were given. Vomiting of dark-brownish material continued at intervals, bleeding from the wound gave trouble, the patient became cyanosed and drowsy as difficulty of respiration developed, his temperature sank to 95·2°, and he died 20¾ hours after being bitten. After death the blood remained fluid but the corpuscles appeared to be intact. The symptoms in this case illustrate well the neurotoxic and haemolytic properties so characteristic of the venom of the Australian Elapine snakes.

A. A.

KOPSTEIN (F.). **Observations on the Effect of the Venom of the Javanese "Green Snake,"** *Lachesis gramineus.—Meded. Dienst d. Volksgezondheid in Nederl.-Indië.* 1928. Vol. 17. Pt. 4. pp. 573–582.

Lachesis gramineus is one of the commoner pit-vipers of Oriental jungles. In this discursive account of the effects of its bite, which begins with a case that occurred in 1863, the systemic effects seem to be negligible, and the local effects to be those generally characteristic of viper-bite, namely haemorrhage, persistent pain, swelling that may spread far from the site of the wound, and a subsequent tendency to gangrene, in bad cases. A. A.

KOPSTEIN (F.). Opmerkingen over de gifwerking van de Javaansche "Groene slang," *Lachesis gramineus.* [**Toxic Effect of the Javanese "Green Snake"** *Lachesis gramineus.*]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1928. Vol. 68. No. 7. pp. 1035–1047.

There are three green snakes, living on trees, in Western Java, where the author carried out his investigations, viz., *Coluber oxycephalus* (non-toxic), *Dryophis prasinus* (slightly toxic) and *Lachesis gramineus* (highly toxic). Records of man being bitten by this snake are rare in those parts. He collected seven cases. In all of them the local symptoms predominated (oedema, excruciating pains, once necrosis and gangrene of the bitten finger). All recovered after treatment with serum. Experiments on susceptible animals (chicken, a squirrel, *Roussethis amplexicaudatus*, house rat, paddy bird) showed that the toxic effect among them was more marked by the general symptoms: affection of the central nervous system. Lizards (*Mabuia multifasciata*) were not susceptible. Nor were snakes (*Tropidonotus piscator*), contrary to their reaction to the poison of *Naja tripudians sputatrix*, to which all snakes, examined by Kopstein, even Naja itself, are highly susceptible.

N. H. Swellengrebel.

ROPPONGI (H.). Toxikologische Untersuchungen ueber das Mamushi-Schlangen-Gift. [**Toxicology of the Venom of the Mamushi** (*Ancistrodon blomhofii*).]—*Fukuoka-Ikwadaigaku-Zasshi* (*Fukuoka Acta Med.*). 1928. Dec. Vol. 21. No. 12. [In Japanese. German summary pp. 109–113.]

The Mamushi (*Ancistrodon blomhofii*) is the only venomous snake of the Japanese Islands proper, and is very common in Kyushu I. The average amount of a single yield of venom is 100 mgm. (33 mgm. dried). Subcutaneous injection of a M.L.D. (=1 mgm. dry venom) into a frog is followed by general haemorrhage around the site of injection, central motor paralysis, and stoppage of the heart. Intravenous injection of a M.L.D. (=1 mgm. of dry venom per kilo. of body-weight) into a guineapig causes at first increased respiration, rise of temperature, appearance of albumin and casts in the urine, leucocytosis, and diarrhoea, and then leucopenia, fall of temperature, dyspnoea, cyanosis, and sudden stoppage first of the breath, then of the heart. If the injection be subcutaneous (=3 mgm. per kilo) there is also bloody oedematous swelling at the site of injection, which may be followed by necrosis with dark sanious discharge.

The effects of Mamushi-bite [presumably in man] are stinging pain locally, with sanguineous oedema, discolouration of the skin, and spreading swelling; dull pain along the course of the lymphatics, fever, headache, and faintness or general languor, diminished urine with albuminuria and casts, and general oedema.

Post-mortem in the guineapig there is evidence of injury to the walls of the blood-vessels (particularly those of the thoracic and abdominal cavities and viscera after intravenous injection of the venom) but not confined to the vessels. The venom in short is described as haemorrhagic.

A. A.

HARA (Y.). **Experimental Studies on the Poisons of Formosan Snakes. I. A Contribution to the Knowledge of the Blood Picture produced by 5 Kinds of Snake Poisons.**—*Taiwan Igakkai Zasshi* (*Jl. Med. Assoc. Formosa.*) 1928. Oct. No. 283. [In Japanese. English summary pp. 69–70.] [Govt. Hosp., Karenko, Formosa, Japan.]

The author gives some details of the effects of the venom of 5 Japanese species of snakes (2 Lachesis, Ancistrodon, Bungarus, Naia) on the corpuscles of the blood of rabbits; and he states that the effects of the venoms of these snakes cannot be differentiated by the blood-pictures alone.

A. A.

KRAUS (R.). Zur Frage der Serumtherapie der Bisse europäischer Vipern. [**Serum-Therapy for Viper-Bite in Europe.**]—*Wien. Klin. Woch.* 1929. Feb. 28. Vol. 42. No. 9. pp. 263–264. With 2 text figs. [State Serotherap. Inst., Vienna.]

The relevant facts recounted in this paper are that the immunizing serum or antivenom for the South American and West Indian Viperid *Lachesis lanceolata* neutralizes not only (as Vital BRAZIL has shown) the venom of other species of South American vipers, but also (as the author and MORITSCH have shown in separate papers abstracted in this *Bulletin*, Vol. 24, p. 404) the venom of the common European viper *V. aspis*.

The object of the present paper is a practical one, namely, to advocate drawing upon the copious supplies of this viper-venom available in South America for the production of an antivenom for the treatment of viper-bite in Europe.

A. A.

OTTO (R.). Vergleichende Untersuchungen mit Schlangengiftseren und Viperngiften verschiedener Herkunft. [**Action of Specific Snake Antivenoms on Alien Viper Venoms.**]—*Ztschr. f. Hyg. u. Infektionskr.* 1928. Dec. 15. Vol. 109. No. 2. pp. 272–285. [2 refs.] [Robert Koch Inst., Berlin.]

In the experiments here tabulated the European viper-antivenom of the Paris Pasteur Institute did not neutralize venom of South American or Javan Crotalinae—with the very doubtful exception of Ancistrodon. The polyvalent antiophidic serum of the Butantan (Brazil) Institute neutralized the venom of the European *Vipera aspis* and of the Javan *Ancistrodon rhodostoma*; and the antibothrops serum of this Institute although it failed of effect against the Javan snake-venom, neutralized the venom of the European viper, but not to

the same degree as the antibothrops serum did. The polyvalent antiviperine serum of the Bandoeng (Java) Institute was active against European viper-venom, by the subcutaneous but not by the intravenous route ; but it did not neutralize the South American crotaline venom. In all these experiments appropriate mixtures of antivenom and venom were injected into guineapigs. [For antecedents of this paper see KRAUS and MORITSCH, this *Bulletin*, Vol. 24, p. 404.]

A. A.

OTTO (R.). Untersuchungen ueber die Toxine europäischer Viperinen. [**Studies of the Venoms of European Vipers.**]—*Ztschr. f. Hyg. u. Infektionskr.* 1929. Feb. 17. Vol. 110. No. 1. pp. 82–92. [3 refs.] [Robert Koch Inst., Berlin.]

The author's experiments, here fully recorded, show that the venoms of the different species of European vipers differ in lethal virulence, in resistance to heat, and in their reactions to foreign antivenoms.

A. A.

GITHENS (Thomas S.) & BUTZ (Lewis W.). **Venoms of North American Snakes and their Relationship.**—*Jl. Immunology.* 1929. Jan. Vol. 16. No. 1. pp. 71–80. [Antivenin Inst. of America, Glenolden, Penn.]

The venoms of six species of rattlesnakes (*Crotalus*) studied by the authors were found to contain identical or almost identical toxic principles. The toxic principles of the Copper-head (*Ancistrodon contortrix*) and moccasin (*A. piscivorus*) are identical with one another, or almost so, but differ to some extent from those of the rattlesnakes. The venom of the dog-faced rattlesnake (*Crotalus terrificus*) of Central and South America and that of the fer-de-lance (*Lachesis atrox*) contain principles that differ entirely from those of the North American rattlesnakes in their antigenous properties. The authors draw attention to the fact that rattlesnake venoms contain in addition to their acutely toxic principles, other components which have the power of binding the antibodies of an immune serum, but are not acutely toxic (to pigeons).

A. A.

BULLETIN OF THE ANTIVENIN INSTITUTE OF AMERICA. Philadelphia, Pa. 1929. Feb. Vol. 2. No. 4. pp. 81–109.

The following items are suitable for notice :—

(1) A short note on a case of a woman bitten (on a finger) by a *barba amarilla* or fer-de-lance (*Lachesis atrox*) nearly six feet long. When brought for treatment nearly 11 hours afterwards she was almost collapsed, and was bleeding freely from wound, mouth, and rectum ; the hand and arm were swollen. An injection of 10 cc. of a specific antivenom was given at once, that and ice to the hand and arm being the only treatment employed. Bleeding did not stop until 24 hours afterwards. The patient was discharged, whole, in ten days. (2) Another, double, case of accident due to a *barba amarilla*. Here a man was bitten (on the leg), and his wound, which was bleeding very freely, was being bathed by his wife, whose fingers were abraded by constant use of a nutmeg grater. The case was being treated by a snake-doctor.

The husband died in two hours, and his wife died, with all the symptoms of *Lachesis atrox* poisoning, the following morning. (3) A note on the venom of a pigmy rattlesnake, *Sistrurus catenatus* which though extremely small in amount (average 5½ to 6 mgm.) is very virulent (0·03 mgm. being the lethal dose for a pigeon). (4) A note on the venom of the spider *Lathrodectes mactans*, an intravenous injection of 0·5 mgm. of which killed a guineapig of 245 gm. " within several hours." (5) A report on a microscopical and chemical examination of a " scorpion stone " said to be good also for snake-bite. A black, porous, odourless, tasteless, coke-like substance burning to a white ash ; specific gravity 1·11 ; capable of absorbing 53·42 per cent. of its own weight of water ; in ultimate analysis bone charcoal. Minute white crystals in its pores are soluble in water and in alcohol and appear to contain a volatile oil of plant origin. (6) A reprint from the *Journal of Immunology* of a paper on the Venoms of North American Snakes and their Relationship a summary of which is given here independently.

A. A.

DE ASSUMPÇÃO (Lucas). Contribuição ao estudo da dosagem dos sôros antipeçonhentos. Confronto entre dosagens pela determinação dos anticoagulinas especificas do plasma e o poder antitoxico do sôro. [**Study of Antivenomous Sera.**]—*Inst. Hyg. de São Paulo Bol. No. 33.* 25 pp. [12 refs.] English summary p. 26. (Reprinted from *São Paulo Medico.* Year 1. Vol. 2. No. 2.)

This is a very technical paper both in substance and in form.

Of the author's conclusions the three which appear to be of general interest are, that there is a direct relation between the toxicity of the venom of *Lachesis lanceolata* and its coagulating power ; but that there is no relation between its toxicity and its neutralizing power in respect of specific antitoxic sera ; and that antitoxic sera possess a proper " individual action " besides their specific power.

A. A.

PHISALIX. Vaccination contre le venin de vipère et la rage expérimentale par les mélanges virus-venin avec excès de virus. [**Vaccination against Viper Venom and Experimental Rabies by Virus-Venom Mixtures.**]—*C.R. Acad. Sci.* 1928. Nov. 26. Vol. 187. No. 22. pp. 1006–1008.

It is known that animals vaccinated against rabies are refractory to the venom of cobra and viper, and *vice versa*—in other words that the virus and the two venoms all three contain both an antigen for rabies and an antigen for venom. In this paper Madame Phisalix gives details of experiments showing that an appropriate mixture of rabies-virus and viper-venom (with the former in excess) inoculated subcutaneously into a rabbit protects the animal both from a lethal dose of viper-venom and from a subdural dose of fixed virus. The duration of the double immunity thus acquired has not yet been determined precisely, but is known to last for several months.

A. A.

KELLAWAY (C. H.). **Snakebite and its Treatment.**—*Health Bull.* Victoria, Australia. 1928. Oct.–Dec. No. 16. pp. 521–525. [Walter & Eliza Hall Inst., Melbourne.]

This is a general summary of existing knowledge, and more particularly of the recent additions to the local knowledge of the subject made by FAIRLEY and other contributors to the Australian " Symposium " now being noticed in this *Bulletin.*

NAUCK (Ernst G.). Untersuchungen ueber das Gift einer Seeschlange (*Hydrus platurus*) des Pazifischen Ozeans. [**Observations on the Venom of the Sea-snake** *Hydrus platurus*.]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1929. Mar. Vol. 33. No. 3. pp. 167–170. [3 refs.] [San Juan de Dios Hosp., San José, Costa Rica.]

Confirmatory evidence that the venom of this sea-snake is purely neurotoxic.

A. A.

REVIEWS AND NOTICES.

NAEGELI (Th.) [Prof. Dr., Bonn.] **A Graphic Guide to Elementary Surgery.** Translated by J. SNOWMAN, M.D., M.R.C.P. With Introduction by Dr. C. GARRÉ, Bonn.—206 pp. With 322 figs. (mostly coloured). 1929. London: John Bale, Sons & Danielsson, Ltd. 83–91, Great Titchfield Street, W. 1. [12s. 6d.]

As the author states in his preface, this book is "an experiment as an introduction to surgery." The book is based on many years personal experience of clinical teaching and follows Garré's methods of tuition. The endeavour is made to enable the student, by means of diagrammatic illustrations, to appreciate better what he sees and hears in his hospital practice. The guiding consideration has been to emphasize the practical aspect of the subject in the "hope that the book may be of some help to the student in appreciating the spirit of surgery, and that the impression he will gain from its pages will be a permanent acquisition."

The opening pages are given to anaesthesia, both general and local. The subject is excellently treated, the essential points well brought out, and these few pages carefully read and practised will save the student many an anxious moment.

The following chapters treat of infection, disinfection, haemorrhage, wounds, inflammation, injuries, diseases of various tissues, tumours, treatment by operation, grafting, and the last chapter, profusely illustrated, is on methods of examination. Some of the illustrations are undoubtedly elementary, others minute in detail, in a few the lesson is not quickly grasped. Some discrepancies are present both in text and illustration that should be rectified: physiological saline quoted as 9 per cent. in the text is rightly shown as 0.9 per cent. on the diagram, the use of the fork in Fig. 104 is not explained, and points 1 and 2 referred to in Fig. 37 are not shown; pronation and supination would be much better illustrated by the fore-arm and hand than by the leg and foot; Trommer's test for sugar is now quite superseded by Fehling's or Benedict's; and dilute acetic acid is generally used in testing urine for albumin as shown in the diagram rather than the strong solution as mentioned in the text.

The description of blood transfusion rather ignores the citrate method and gives the impression that the direct method is more frequently used; nor is the needle method which avoids exposing the donors' or recipient's veins shown. The formidable array of instruments for vein exposure shown in the illustration has not been found necessary in tropical work. The need of selecting donors free from syphilis or malaria might be stressed.

The statements that "animal parasites are of comparatively small importance in surgery" and that "in certain rare cases elephantiasis is the result of obstruction of the lymphatic vessels by parasites" do not accord with tropical practice. Elephantiasis can hardly be described as rare and the surgery necessitated by the ravages of *F. bancrofti* can be considerable. Hydatid disease and ascariasis as calling for surgical intervention are mentioned, but amoebic abscess of the liver is not noticed.

The author is to be congratulated on providing a clear and concise exposition of the main elementary points of surgery that will help those whose duty it is to teach, and from the pages of which, every careful student is bound to gain "some useful permanent acquisition."

A comprehensive index concludes the work.

W. E. Cooke.

MAYER (Martin) [Professor Dr., Abteilungsvorsteher am Institut für Schiffs- und Tropenkrankheiten. Privatdozent an der Universität Hamburg.] **Exotische Krankheiten. Ein Lehrbuch für die Praxis.** [Text Book on Exotic Diseases.] 2nd Edition.—pp. vii+368. With 252 figs. & 3 coloured plates. 1929. Berlin: Verlag von Julius Springer. [Rm. 39: gebunden Rm. 40·80.]

The first edition of Professor Martin Mayer's book was reviewed in these columns in 1924; this new edition is on the same lines as its predecessor, but a considerable amount of new matter has been added; in spite of this, the book is still of a convenient size. Although there is much compression, nothing of any importance seems to have been omitted; but it is a book that must be read with concentrated attention, for there is no idle padding.

The author has devoted most of his rather limited space to symptoms and treatment; his aim has been to make the book a practical one. The details of zoological descriptions and taxonomy have been omitted deliberately; for them Professor Mayer refers the reader to systematic works on these subjects; and, indeed, such lengthy matters are somewhat out of place in a general textbook of tropical medicine.

Some of the articles on tropical diseases of the skin, animal poisons, snakebite, and the effects of tropical heat are too summary to be of much use; but, with these exceptions, the book is an admirable one. Where all are good, it is difficult to select any particular articles for special commendation, but those on amoebic dysentery, abscess of the liver and yellow fever are fine pieces of work. There are many excellent photographs and other illustrations.

To those who read German, and who want a thoroughly reliable book on tropical diseases, which will not take up too much space in their libraries, this one can be recommended with confidence.

H. J. Walton.

CHAMBERLAIN (Weston P.) [Colonel, Med. Corps., U.S. Army, Chief Health Officer, the Panama Canal.] **Twenty-Five Years of American Medical Activity on the Isthmus of Panama 1904-1929. A Triumph of Preventive Medicine.**—74 pp. With 23 plates & 2 maps. 1929. The Panama Canal Press. Mount Hope, C.Z.

The pioneer in the scheme of constructing a ship canal across the Isthmus of Panama was the great Cortés, and as early as 1529 plans for such a project were drawn up. A few years later Charles V of Spain, had further surveys carried out in order to determine the most advantageous course for the proposed canal, and the scheme was again revived in 1616 by Philip II. During the eighteenth century all efforts to commence the undertaking came to nought, and it remained for the closing years of the nineteenth century to call forth the first serious attempt to carry a waterway through the Isthmus. De Lesseps' ill-fated project failed, as we know, mainly through the ravages of tropical diseases now considered preventable. Between 1881 and 1889, in a force of white employees averaging 1,600 in number there were 2,000 deaths from yellow fever alone, while in the whole force, with an average strength of 10,000, the total mortality reached the appalling figure of 16,000 in the same period.

In 1904 the United States assumed full jurisdiction over the Canal Zone (a strip approximately five miles broad on each side of the waterway) and, as a necessary part of their health projects, they obtained complete sanitary control of the Panaman cities of Panama and Colon, adjacent to the extremities of the Canal. The subsequent medical history, especially the dramatic conquest of yellow fever, is in general well known. Contrary, however, to what is often stated, there has been no attempt to free the entire

Canal Zone from malaria, a labour that would cost years of effort and millions of dollars. Anti-malaria work is confined to the more important towns and their environs, but even so, this has effected a fall in the malaria incidence rate from 821 per thousand in 1906, to 16 per thousand in 1916, while the death rate has dropped from 7·25 to nil. Since 1916 there has been little further diminution of malaria in spite of an extension of the area under sanitary control. Seemingly the benefits of the new works are offset by the larger number of infections now acquired in non-sanitated districts, for which increased motoring facilities are mainly responsible.

The Health Department, under a Chief Health Officer, is divided into three sections—Hospitals, Sanitation, and Maritime Quarantine, and its present policy is to recruit the staff from the Army Medical Service as far as possible. For several years past the amount voted annually by Congress for the Public Health Service has been $670,000, to which are added for expenditure the earnings of the Health Department for the year, so that the sum available in 1928 was $1,500,000, of which $116,000 was spent on strictly anti-mosquito work. It is interesting to note that the famous Panama larvicide has been largely discarded in favour of the cheaper and more effective fuel oil which is preferred also to Paris green. Sanitarians may be surprised to hear that the costly modern refuse destructors have been closed, and incineration of garbage replaced by burial, using crude oil to prevent fly-breeding. This method of disposal is stated to be more economical and more effective than burning. Stable manure is composted in concrete pits, after which it may be employed as fertilizer by permission of the Health Department. The use of fresh manure is forbidden. As a result of these measures the Isthmian towns are so free from flies that traps and poisons are rarely required.

The brochure is well illustrated with photographs and maps, and appended there is a bibliography of medical and allied publications dealing with Panama.

W. P. MacArthur.